

# N-Terminal Pro-Brain Natriuretic Peptide as a Predictor of Complication and Mortality in Acute ST Segment Elevation Myocardial Infarction

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## ABSTRACT

**Introduction:** Coronary artery disease and its end result, myocardial infarction continues to be a significant cause of mortality and morbidity in the world. Over the past 50 years, it has become clear that the cascade of thrombotic events following atherosclerotic plaque rupture causes occlusion of the coronary artery, interrupting blood supply and oxygen to myocardium thus resulting in infarction. So Study aimed to assess the relationship between N-terminal pro-Brain Natriuretic Peptide levels on admission in ST elevation myocardial infarction (STEMI) and its short term complications

**Material and Methods:** A total of 40 patients, who present with acute ST elevation myocardial infarction within 12 hrs to Rajendra Institute of Medical Sciences, were included in this study. NT-ProBNP and other routine cardiac evaluations at the time of admission were determined. The patients were followed over a period of 7 days for development of various short term complications of acute MI.

**Results:** Among the complications arrhythmias comprised the majority with 22.5% (9 subjects). 5 patients (12.5%) succumbed to death. NT-proBNP levels in the full cohort ranged from 246 to 3000 p g/ ml. The mean levels were 1585.6 5±99 9.1 33 p g/ ml with the median NT-proBNP as 1483.50 pg/ml. NT-proBNP cutoff of 1691.50 pg/ml has 100% sensitivity and 88.9% specificity in predicting the occurrence of complications in STEMI.

**Conclusion:** NT-proBNP is a strong predictor of short term outcome in AMI, including death.

**Keywords:** Acute STEMI, NT-proBNP, Prognosis, Complication, Death

## INTRODUCTION

The history of ischemic heart disease is relatively brief and represents a very convincing example of the rapid development of cardiology as a scientific discipline.<sup>1,2</sup>

A syndrome of prolonged, severe chest pain was first described in the medical literature in 1912 by James Brian Herrick, who attributed the syndrome to coronary thrombosis, the development of a clot in a major blood vessel serving the heart. As a result, the disorder was termed coronary thrombosis or coronary occlusion (blockage of a coronary artery), but the precise diagnosis was possible only after the introduction of the electrocardiogram into clinical practice in the 1920s.

Coronary artery disease (CAD) and its end result, myocardial infarction (MI) continue to be a significant cause of mortality and morbidity in the world. Over the past 50 years, it has become clear that the cascade of thrombotic events following atherosclerotic plaque rupture causes occlusion of the coronary artery, interrupting blood supply and oxygen to myocardium thus resulting in infarction. Myocardial necrosis following

infarction is followed by heart failure, myocardial rupture or arrhythmias. Early treatment of myocardial ischaemia to prevent necrosis with treatments such as fibrinolysis, coronary artery bypass grafting and percutaneous coronary intervention has improved outcome.<sup>3</sup>

Optimal risk stratification of patients with acute myocardial infarction is of paramount importance to deliver appropriate care. Risk prediction based on clinical, Electrocardiography (ECG), and biochemical i.e., cardiac troponin, Creatinine Kinase-MB, however is relatively inaccurate.<sup>4</sup>

BNP consists of 32 amino-acids, with a central ring of 17 amino-acids created by a disulphide bond between cystine bases. It is synthesized as an inactive pro-hormone that is split into the active hormone BNP and the inactive N-terminal fragment (NT-proBNP).<sup>5,6</sup> [Figure. 1] BNP has a number of systemic effects, including vasodilatation, increase in urinary volume and sodium output and inhibition of the sympathetic nervous system and the renin-angiotensin-aldosterone system.<sup>7</sup> It is widely believed that predominant pathophysiological process underlying increased circulating levels of BNP and NT-proBNP is regional or global impairment of left ventricular systolic or diastolic function leading to left ventricular wall stretch.<sup>8</sup> In addition, their increased levels may also result directly from cardiac ischaemia. It appears that ischaemic or injured myocardial tissue releases extra BNP irrespective of haemodynamic factors.<sup>9,10</sup>

Assessing NT-proBNP is easier than BNP. The clearance of BNP is rapid by way of several mechanisms. The clearance of NT-proBNP is mainly by passive kidney excretion, and hence it remains elevated for longer time.<sup>10</sup>

Levels of BNP and NT-proBNP correlate with left ventricular dilatation, remodeling, and dysfunction in patients after acute myocardial infarction (MI).<sup>11</sup> In patients with acute MI, the increase in NT-pro-BNP is greater than the increase in BNP and has a higher discriminative value for early cardiac dysfunction than BNP, suggesting that it may be a more sensitive marker of left ventricular dysfunction.<sup>12</sup> Plasma NT-proBNP level has been shown to provide valuable prognostic information on short

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– and long-term mortality in patients with acute MI. Study aimed to assess the relationship between N-terminal pro-Brain Natriuretic Peptide levels on admission in ST elevation myocardial infarction (STEMI) and its short term complications and to determine the value of NT-proBNP in predicting short term outcome in patients with STEMI.

**MATERIAL AND METHODS**

**Source of data**

A total of 40 patients, of different ages, who present with acute ST elevation myocardial infarction, were included in this study. The data were collected over duration of one year from July 2013 to June 2014 after taking informed consent. The approval of institutional ethics committee was taken prior to the commencement of this study.

The study was a cross-sectional study and the method of sampling used was purposive.

**Method of collection of data**

A total of 40 patients, who present with acute STEMI to Rajendra Institute of Medical Sciences, were included in this study based on inclusion exclusion criteria.

The patients were evaluated as per the history, general physical examination, systemic examination, ECG, cardiac troponin-T, urea, creatinine, NT-proBNP at the time of admission and Echocardiography within 7 days of admission. The included patients were followed up over a period of 7 days for development of various short term complications of acute MI.

**Inclusion Criteria**

Those admitted in Rajendra Institute of Medical Sciences, Ranchi having:

1. Typical ischaemic symptoms and ST segment elevation of at least 1 mm in 2 or more ECG leads.
2. Admitted within 12 hours after onset of symptoms.
3. Patients within the age group of 30-80 years.

**Exclusion Criteria**

1. STEMI patients with previous chronic heart failure.
2. Chronic kidney disease, cardiogenic shock at presentation.
3. Who present 12 hours after the onset of symptoms.
4. Who are taken up for angioplasty within 7 days of study period.
5. Age < 30 years or > 80 years.
6. Non ST segment elevation MI and unstable angina.

**STATISTICAL ANALYSIS**

Data were computer analyzed using MedCalc statistical package. Mean and standard deviation was calculated. Data will be analyzed for the statistical significance using Karl Pearson correlation coefficient, Mann Whitney test, 't' test, and by Receiver Operating Curve (ROC) analysis. A p value of <0.05 was considered significant.

**RESULTS**

A total of 40 patients who presented with acute ST elevation myocardial infarction to Rajendra Institute of Medical Sciences, were studied. 70% were males and 30% were females. The male to female ratio was 2.33:1. Majority was in the age group of 50-70 yrs (67.5%). 35% belonged to 51-60 age group, followed by 32.5% in the 61-70 age group. The mean age was 58.73. Out of 40 subjects, 23 (57.5%) were smokers. The relation between smoking and NT-proBNP was not statistically significant.

Out of the 40 patients studied 45% of the patients had ALWMI, 15% had ASMI, 32.5% with IWMI and 7.5% with IWMI+RWMI.

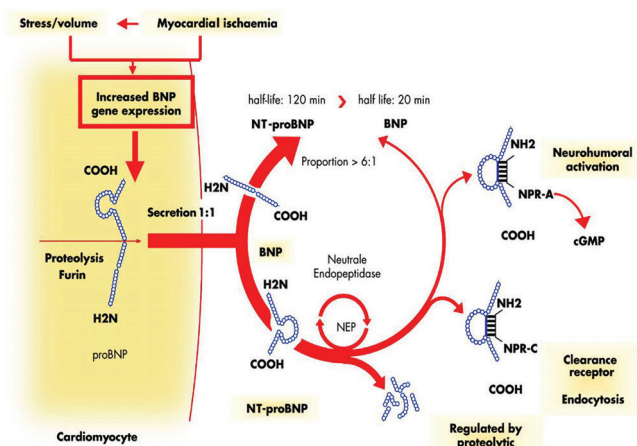
NT-pro BNP levels in the full cohort ranged from 246 to 3000 pg/ml. The mean levels were 1585.65±999.13 pg/ml with the median NT-proBNP as 1483.50 pg/ml.

Out of the 40 patients studied 13 patients (32.5%) had complication and 27 were free from any complications. [Figure 2] Arrhythmias comprised the majority with 22.5% (9 patients). 5 patients succumbed to death (12.5%). However, the association of NT-ProBNP level with conduction block and left ventricular thrombus was not found to be significant. There was a significantly higher incidence of arrhythmias (9 patients, p= 0.001), cardiac failure (4 patients, p= 0.043), lower ejection fraction (p<0.020) and deaths (5 patients, p= 0.024) in the group who had above median NT-proBNP values.[Figure 3], [Table 1]. All 13 patients who had complications belonged to the above median NT-proBNP group (p <0.0001).

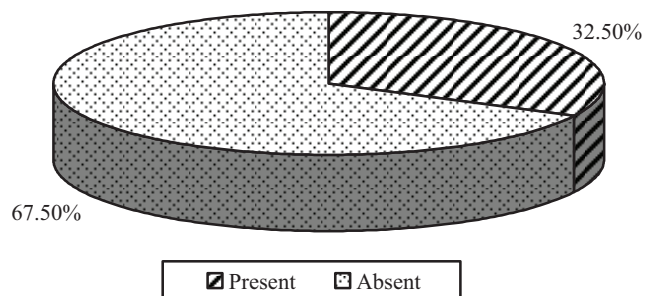
The relation between the cardiac troponin-T values, NT-proBNP values, complications and deaths were not statistically significant.

There was no statistical significance in the relation between LVEF <50% and the occurrence of complications, deaths. However there was strong correlation between LVEF<50% and NT-proBNP above the median (p= 0.020).

In the full study cohort, NT-proBNP above median emerged as the strong predictor of worsening heart failure, occurrence of arrhythmias and deaths within 1 week study period. NT-proBNP below median emerged as a strong predictor for freedom from



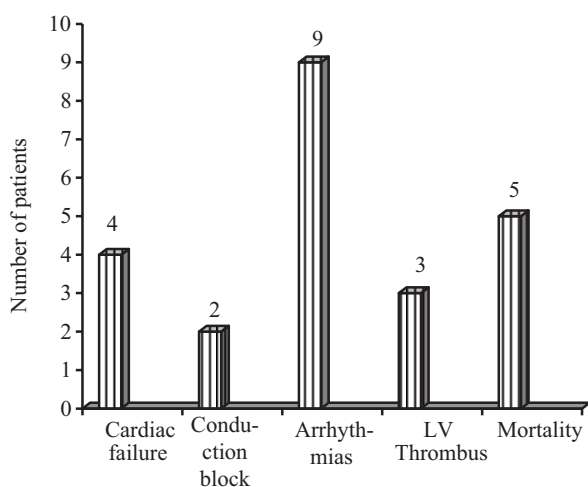
**Figure-1:** Schematic illustration of B-type natriuretic peptide (BNP) and NT-proBNP synthesis, release and receptor interaction



**Figure-2:** Proportion of complications in the patients

Complications		NT-ProBNP value			p value
		<1483.50	>1483.50	Total	
Cardiac failure	Absent	20	16	36 (90%)	0.043
	Present	0	4	4 (10%)	
Conduction block	Absent	20	18	38 (95%)	0.244
	Present	0	2	2 (5%)	
Arrhythmias	Absent	20	11	31 (77.5%)	0.001
	Present	0	9	9 (22.5%)	
LV Thrombus	Absent	20	17	37 (92.5%)	0.344
	Present	0	3	3 (7.5%)	
All complications	Absent	20	7	27 (67.5%)	0.0001
	Present	0	13	13 (32.5%)	
Mortality	Absent	20	15	35 (87.5%)	0.024
	Present	0	5	5 (12.5%)	

**Table-1:** Tabular analysis of results with its significance



**Figure-3:** Frequency of various complications in the patients

adverse events.

## DISCUSSION

BNP has been used to provide prognostic information in patients with acute coronary syndrome (ACS). Current knowledge indicates that NT-proBNP may be a more sensitive and an effective prognostic tool in these patients.<sup>12</sup>

In the present study we have demonstrated that NT-proBNP is a powerful predictor of adverse outcomes including mortality within 1 week in the patients presenting with STEMI. NT-proBNP levels in our study varied according to the infarct size and there was a wide scatter in the NT-proBNP levels presumably based on the extent of myocardial damage and functional impairment which directly correlates with adverse outcomes including mortality. Similar scatter has been observed in other studies also.<sup>4</sup> It is challenging to derive any prognostic cut-off value, implying that a single cut-off level cannot be used for NT-proBNP in the AMI population.<sup>12</sup> In clinical studies, natriuretic peptide concentrations have been reported as levels above or below the median value observed in the population under study, thus permitting a dichotomous approach to interpretation of the results.<sup>2,11</sup> In the present study the median level of NT-proBNP was 1483.50 pg/ml. It was found that there was a significantly higher incidence of arrhythmias ( $p=0.001$ ), cardiac failure ( $p=0.043$ ), lower ejection fraction ( $p<0.020$ ) and deaths ( $p=0.024$ ) in the group who had above median NT-

proBNP values.[Table 1] All 13 patients who had complications belonged to the above median NT-proBNP group ( $p<0.0001$ ).

In the full study cohort, NT-proBNP above median emerged as the strong predictor of worsening heart failure, occurrence of arrhythmias and deaths within 1 week study period. NT-proBNP below median emerged as a strong predictor for freedom from adverse events.

NT-proBNP measurement as a prognostic test has a distinct advantage over other currently available parameters since it is a quantitative test with precise values and is not operator-dependent, like the 2D Echo. The test doesn't have the drawbacks of inter and intra-observer variability in quantifying the data obtained. Our study, like many recent works, measured NT-proBNP instead of BNP due to its superior predictive value. Our results for NT-proBNP confirm and extend observations made regarding the prognostic value of NT-proBNP in patients with AMI.

## CONCLUSIONS

- NT-proBNP is a strong predictor of short term outcome in AMI, including death. NT-proBNP is a better short term prognostic indicator than
- cardiac troponin-T and LVEF. It is a good tool for the risk stratification of acute MI patients so that appropriate treatment strategies could be
- planned.

## REFERENCES

1. Braunwald E. The Simon Dack lecture. Cardiology: The past, the present, and the future. *J Am Coll Cardiol.* 2003;42:2031-41.
2. Stanek V. Progress in the therapy of ischemic heart disease, *Kapitolyzkardiologie.* 2002;4:3-11.
3. Chan D, Ng LL. Biomarkers in acute myocardial infarction. *BMC Med.* 2010;7:34.
4. Galvani M, Ottani F, Oltrona L, Ardissino D, Gensini GF, Maggioni AP, et al. N-Terminal Pro-Brain Natriuretic Peptide on Admission Has Prognostic Value Across the Whole Spectrum of Acute Coronary Syndromes. *Circulation.* 2004;110:128-134.
5. Julian DG. Treatment of cardiac arrest in acute myocardial ischaemia and infarction. *Lancet.* 1961;14;2:840-4.
6. Tsekoura DK, Karavidas AI, Raisakis KG, Zacharoulis AZ. Brain Natriuretic Peptide. *Hellenic J Cardiol.* 2003;44:266-270.

7. Ezekowitz JA, Thérroux P, Chang W, Mahaffey KW, Granger CB, Weaver WD, et al. N-terminal pro-brain natriuretic peptide and the timing, extent and mortality in ST elevation myocardial infarction. *Can J Cardiol.* 2006;22:393-397.
8. Hall C. NT-Pro BNP: The Mechanism behind the marker. *J Card Fail.* 2005;11(5 Suppl):S81-S83.
9. Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-ProBNP in clinical routine. *Heart.* 2006;92:843-849.
10. Goetze JP, Christofferson C, Perko M, Arendrup H, Rehfeld JF, Kastrup J, et al. Increased cardiac BNP expression associated with myocardial ischaemia. *FASEBJ.* 2003;17:1105-1107.
11. Mega JL, Morrow DA, deLemos JA, Sabatine MS, Murphy SA, Rifai N, et al. B-type natriuretic peptide at presentation and prognosis in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol.* 2004;44:335-339.
12. Puri A, Narain V, Mehrotra S, Dwivedi S, Saran R, Puri V. N-Terminal-ProBrain Natriuretic Peptide as a Predictor of Short-Term Outcomes in Acute Myocardial Infarction. *Ind Heart J.* 2005;57:304-310.

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