

Original Research Article

B-type natriuretic peptide levels and its correlation with left ventricular functions and heart failure in patients of acute coronary syndromes

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ABSTRACT

Background: This study was designed to measure levels of B-type natriuretic peptide (BNP) across entire spectrum of acute coronary syndrome (ACS) and to find its correlation with left ventricular functions and heart failure.

Methods: We measured BNP levels at baseline in 100 consecutive patients between 24-96 hours after the onset of ischemic symptoms in patients of ACS. Echocardiography was performed in all patients between day 2-5 after the index diagnosis and stabilizing the patients.

Results: The BNP levels were raised across the entire spectrum of ACS, with levels (>80 pg/ml) in 32.2% of patients with ST segment-elevation myocardial infarction (STEMI), in 24% with non-ST segment-elevation myocardial infarction (NSTEMI), and in 16.6% with unstable angina (UA) respectively. High BNP levels were associated with greater increase in LV end-systolic volumes ($r=+0.545$, $p<0.001$) (LVESV) and end-diastolic volumes (LVEDV) ($r=+0.336$, $p<0.001$). There was a negative correlation between BNP levels and left ventricular ejection fraction (LVEF) ($r=-0.394$, $p<0.002$). BNP levels were significantly raised (156.0 ± 45.1 vs 57.7 ± 18.3 pg/ml, $p<0.02$) in patients developing symptomatic clinical heart failure, irrespective of LVEF $\leq 40\%$.

Conclusions: Integrated use of echocardiography and BNP levels provide powerful incremental assessment of cardiac functions, clinical status, and outcome across the entire spectrum of acute coronary syndromes (ACS). Increased BNP levels are associated with progressive ventricular dilatation, LV-dysfunction, development of clinical heart failure and is associated with poor prognosis in patients of ACS.

Keywords: BNP, ACS, STEMI, NSTEMI, UA, CHF, LVESV, LVEDV, LVEF, ECG

INTRODUCTION

Brain (B-type) natriuretic peptide is a cardiac neurohormone synthesized in ventricular myocardium and released into the circulation in response to ventricular dilatation and pressure overload.¹⁻³ BNP is synthesized in bursts and constitutively released from ventricular myocytes as a 76-amino acid N-terminal fragment (N-terminal BNP) and a 32-amino acid active hormone (BNP).⁴ The actions of brain (B-type) natriuretic peptide,

include natriuresis, vasodilatation, inhibition of the renin-angiotensin-aldosterone axis, and inhibition of sympathetic nerve activity.⁵ The plasma level of B-type natriuretic peptide is elevated in patients with congestive heart failure and increases in proportion to the degree of left ventricular dysfunction and the severity of symptoms of heart failure.^{2,6} The concentration of BNP is higher in patients with systolic than with isolated diastolic dysfunction, and highest in those with both systolic and diastolic dysfunction.⁷ After acute myocardial infarction,

a raised concentration of BNP identifies patients at increased risk for adverse left-ventricular remodelling, left-ventricular dysfunction heart failure and death, independent of age, history of heart failure and left ventricular ejection fraction.⁸⁻¹⁰ Patients with BNP levels of >80 pg/ml were significantly more likely to die, have new or recurrent MI, or have new or progressive heart failure than those with levels of 80 pg/ml or less.¹¹⁻¹³

After acute myocardial infarction, levels of B-type natriuretic peptide rise rapidly during the first 24 hours and then tend to stabilize.¹⁴⁻¹⁷ First studied as a diagnostic and prognostic marker among patients with congestive heart failure (CHF), BNP was subsequently found to predict outcomes in patients with acute transmural myocardial infarction (MI).^{18,19} We extended these findings across the spectrum of patients with ACS including those with UA.

Aim and objectives

Aim and objectives of the study were to measure the plasma level of BNP in patients of acute coronary syndromes (ACS) and to find correlation between plasma BNP levels and left ventricular function and heart failure in patients of ACS.

METHODS

A total of 100 consecutive patients of ACS admitted in medical intensive coronary care unit (MICCU) from January 2008 to January 2009, of govt. medical college (GMC-Srinagar), fulfilling the inclusion criteria were included in the study.

Study design

The study design was prospective and cross-sectional-analytical study.

Statistical analysis

Data was expressed as mean \pm SD and percentage. The inter-group relation was determined by using chi-square, student 't', Mann Whitney 'U' test and odd's ratio analysis. Pearson correlation analysis was used to assess the association of BNP levels and LV function. P value of <0.05 was considered significant. Software MS excel, Minitab and SPSS 11.5 were used for drawing valid inferences.

Inclusion criteria¹¹

Patients were included if they presented within 72 hours after the onset of ischemic discomfort and met one or more of the following criteria:

Electrocardiographic changes (ST-segment depression or elevation of at least 0.5 mm, T-wave inversion of at least 3 mm in at least three leads, or left bundle-branch block),

elevated levels of cardiac markers, a history of coronary disease, or an age of at least 65 years in patients with diabetes or vascular disease.

Exclusion criteria

Patients were excluded if age >80 years, death within 24 hours after acute coronary syndromes, cardiogenic shock and serum creatinine >2.5 mg/dl.

A detailed history and clinical examination of all the patients fulfilling above inclusion criteria with baseline investigations was done. Heart failure was diagnosed on the basis of Framingham's criteria for diagnosis of congestive heart failure.²⁰

Biochemical analysis

Blood sample (2 ml) were taken between 24 to 96 hours of the onset of the symptoms. BNP was measured in EDTA. Anticoagulated plasma using two site sandwich immunoassays by direct chemiluminescence technology using ADVIA-CENTAUR from SIEMENS). This assay has a minimal detectable concentration of 2.0 pg/ml.

Echocardiography

Two-dimensional M-mode and colour flow Echocardiogram were obtained with echocardiographic equipment power vision 8000 Toshiba Japan between day 2 and 5 after acute coronary syndrome operating at 2.5 MHz, adult probe. Two-dimensional imaging examination were performed in the standard fashion in parasternal long and short axis views and apical 4 and 2-chamber views. Two-dimensional echocardiogram was subjected to careful visual analysis to detect regional contractile abnormalities. Left Ventricular end systolic volume (LVESV), Left ventricular end diastolic volume (LVEDV) and ejection fraction (EF%) were derived from biplane apical (4-and 2-chamber) views with use of a modified Simpson's rule algorithm. All recording and measurements were obtained by the same observer according to the recommendations of American society of echocardiography. On the basis of LVEF patients were divided into two groups patients with EF \leq 40% and EF>40%.²¹

RESULTS

A total of 100 patients were included in the study, out of which 69% were males and 31% were females. 40% patients were >65 year of age and 60% patients \leq 65 years. 83% Patients were in Killip class I, 14% in Killip class II, 3% in Killip class III and patients in Killip class IV were excluded from study. Cigarette smoking in 67% (33%-current smoker and 34%-past smoker), hypertension in 62%, diabetes mellitus in 26% and history of angina in 42% are major risk factors in our study. The demographic data as per age, sex, clinical signs, Killip class, and past medical history at the time of presentation are depicted in Table 1.

Table 1: Demographic data as per age, sex, clinical signs, Killip class, and past medical history at the time of presentation.

Baseline characteristics of the patients included in the study			
Patient characteristics		No. of patients	Percentage (%)
Gender	Male	69	69
	Female	31	31
Age (year)	≤65	60	60
	>65	40	40
Heart rate (mean±SD)	84.9±14.3 (62-136)		
Systolic blood pressure (mean±SD)	132.3±21.0 (90-190)		
Killip class	Class I	83	83
	Class II	14	14
	Class III	03	03
Past medical history			
Cigarette smoking		67	67
Diabetes mellitus (DM)		26	26
Hypertension		62	62
Congestive heart failure (CHF)		05	5
Previous angina		42	42
Cerebrovascular disease (CVD)		05	5

Table 2: Index diagnosis: 59% patients had STEMI, 29% had NSTEMI and 12% had UA.

ACS in patients included in the study		
ACS	No. of patients	Percentage (%)
STEMI	59	59
NSTEMI	29	29
UA	12	12

Table 3: Out of total 100 patients included in the study; 28% patients were found to have BNP levels >80 pg/ml with mean BNP levels of 68.7±48.5 pg/ml.

BNP levels (pg/ml) in patients of ACS included in the study		No. of patients	Percentage (%)
BNP levels (mean ± SD)		68.7±48.5 (2,634)	
Brain BNP	>80	28	28
	≤80	72	72

Table 4: 32.2% of patients with STEMI, 24.1% with NSTEMI and 16.6% with UA had BNP levels >80 pg/ml.

Brain BNP levels in relation with acute coronary syndromes in the studied patients				
Acute coronary syndrome	>80		≤80	
	N	%	N	%
STEMI	19	32.2	40	67.8
NSTEMI	7	24.1	22	75.9
U/A	2	16.6	10	83.4
Overall chi square (χ^2) =1.496; p=0.473				

Table 5: The mean LVESV, LVEDV were significantly high, whereas LVEF was significantly low in patients with BNP levels >80 pg/ml.

LV functions in the studied patients of ACS with respect to BNP levels			
LV function	>80	≤80	P value
LVESV (ml)	67.2±19.7 (48, 117)	52.5±8.8 (31, 80)	0.001
LVEDV (ml)	124.0±24.0 (84, 180)	107.9±19.6 (62, 156)	0.001
LVEF (%)	42.3±7.6 (35, 60)	50.7±7.2 (30, 65)	0.009

Table 6: The mean BNP levels were significantly more in patients with LVEF <40% and clinical heart failure compare to patients without clinical heart failure, though LVEF<40%.

Comparison of BNP levels according to development of clinical heart failure and LVEF				
Clinical heart failure	EF ≤40		EF >40	
	BNP (pg/ml)	N	BNP (pg/ml)	N
Present	156.0±45.1	11	115.5±43.3	6
Absent	57.7±18.3	4	43.3±30.9	79
P=0.02 (Sig.)		P=0.026 (Sig.)		

The index diagnosis was STEMI in 59%, NSTEMI in 29% and UA in 12% respectively. STEMI patients were maximum in our study, as diagnosis is based on ECG findings only, and 24-hour availability of ECG (Table 2). 28% patients were found to have BNP levels >80 pg/ml and 62% had BNP levels ≤80 pg/ml (Table 3). 32.2% of patients with STEMI, 24.1% with NSTEMI and 16.6% with UA had BNP levels >80 pg/ml. BNP levels >80 pg/ml were more (32%) in patients with STEMI, as

STEMI patients are more critical and have higher mortality compared to NSTEMI and UA patients (Table 4). The mean LVESV, LVEDV were significantly higher, whereas LVEF was significantly low in patients with BNP levels >80 pg/ml. Higher LVESV and LVEDV are associated with higher BNP levels (>80 pg/ml) as higher volumes are associated with more stretch on ventricular wall, which is major factor for release of BNP (Table 5).⁴ The mean BNP levels were significantly more (156.0 vs 57.7 pg/ml) in patients with LVEF <40% and clinical heart failure compare to patients without clinical heart failure, though LVEF<40% (Table 6). There is a significant positive correlation between BNP levels and LVESV, LVEDV, whereas there is significant negative correlation between BNP levels and LVEF (Table 7).

Table 7: There is a significant positive correlation between BNP levels and LVESV, LVEDV, whereas there is significant negative correlation between BNP levels and LVEF.

Correlation of BNP levels with left ventricular functions		
LV functions	R	P value
LVESV (ml)	+0.545	0.001 (Sig)
LVEDV (ml)	+0.336	0.001 (Sig)
LVEF (%)	-0.394	0.002 (Sig)

DISCUSSION

This was the first ever study of its kind conducted in our state (Jammu and Kashmir) where we measured BNP levels, a cardiac neuro-hormone across the entire spectrum of ACS. After adjustment for other independent predictors of long-term risk of death, a BNP threshold of more than 80 pg/ml was taken as cut off for evaluation in this study.¹¹

Among 100 patients of ACS, index diagnosis was STEMI in 59%, NSTEMI in 29% and UA in 12%. In our study 32.2% of the patients with STEMI, 24% of the patients with NSTEMI and 16.6% of the patients with UA had BNP levels>80 pg/ml. This shows that BNP levels were raised among all the three subgroups of ACS patients, with STEMI patients more likely to have raised BNP levels >80 pg/ml.^{12,13}

Left ventricular functions were measured in all patients between day 2-5 of ACS. The LVESV (67.2±19.7 vs 52.5±8.8 ml; p<0.001), LVEDV (124.0±24.0 vs 107.9±19.6 ml; p<0.001), were significantly increased in patients with BNP levels >80 pg/ml as compared to patients with BNP levels ≤80 pg/ml. On contrary LVEF was significantly low (42.3±7.6 vs 50.7±7.2 %; p<0.009) in patients with BNP >80 pg/ml as compared to those with BNP levels ≤80 pg/ml. High BNP levels were associated with greater increase in LV end-systolic (r=+0.545, p<0.001) and end-diastolic volumes (r=+0.336, p<0.001). There was a negative correlation between BNP levels and LVEF (r=-0.394, p<0.002).²¹

The mean BNP levels were significantly more 156.0 pg/ml in patients with clinical heart failure and EF≤40% compared to patients with mean BNP 57.7 pg/ml in whom clinical heart failure was absent though EF≤40%. Similarly mean BNP levels were more 115.5 vs 43.3 pg/ml in patients with clinical heart failure and EF >40% compared to patients in whom clinical heart failure was absent though EF >40%. The BNP levels were significantly higher in patients with clinical heart failure irrespective of LVEF.

Limitations

LV-diastolic functions were not assessed. Further studies should be done on larger scale including measurement of LV-diastolic dysfunctions.

CONCLUSION

Integrated use of echocardiography and BNP levels provide powerful incremental assessment of cardiac functions, clinical status, and outcome across the entire spectrum of ACS. High levels of BNP are a powerful marker of LV systolic dysfunctions, development of clinical heart failure and poor prognosis in patients of ACS.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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