

B-Type Natriuretic Peptide (BNP) and Left Ventricular (LV) Function in Patients with ST-Segment Elevation Myocardial Infarction (STEMI)

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Conflict of interest notification page: "I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work."

ABSTRACT

Background: After acute myocardial infarction (AMI), left ventricular (LV) function is a well-established prognostic marker. Recent studies indicate that serum levels of brain natriuretic peptide (BNP) also represent an prognostic marker in this setting but so far without a precise cut-off value.

Objective: The aim of this study was to assess the predictive value of BNP serum levels for LV function assessed by echocardiography in STEMI patients undergoing revascularization.

Methods: We prospectively studied a cohort of 88 consecutive patients (mean age 51.6 years, 88.6% males) hospitalized in our clinic for STEMI in Killip class I (50% anterior infarction), who underwent reperfusion therapy. Serum BNP levels were measured on admission, at 24h and at 30 days after reperfusion. Detailed echocardiography was performed at baseline, at 24 hours after reperfusion, on discharge and at follow-up at 1 month. Left ventricular systolic and diastolic dysfunction were defined by LVEF < 45% and E/A ratio respectively.

Results: ROC curve analysis showed that BNP measurements on admission and at 24 hours after revascularization have no predictive value neither for diastolic LV dysfunction in anterior or inferior AMI patients, nor for systolic LV dysfunction in inferior AMI patients. Only BNP levels at 24 hours after revascularization can predict systolic LV dysfunction in anterior AMI patients with a 90.3% sensitivity and a 60% false positive rate at a cut off value of 90pg/ml.

Conclusions: Early measurement of BNP levels may allow early prediction of anterior STEMI patients at risk of developing systolic LV dysfunction after revascularization therapy.

Keywords: myocardial infarction, brain natriuretic peptide (BNP), revascularization, LV dysfunction

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BACKGROUND

Early and successful myocardial reperfusion by primary percutaneous coronary intervention or by thrombolysis is the most effective strategy for reducing the infarct size and improving clinical outcome in STEMI patients (1).

Serum levels of brain natriuretic peptide (BNP), a cardiac neurohormone that is synthesized in ventricular myocardium and released in response to increased ventricular wall stress (3-6), are elevated both in patients with heart failure and acute coronary syndromes – acute myocardial infarction (AMI) and unstable angina, and represent an important marker of clinical outcome and cardiovascular mortality in patients with myocardial infarction, of recent research interest (7-12).

Previous studies had shown the prognostic value of BNP, measured in the subacute phase (13-15) on mortality of STEMI patients, while the value of early measurements of BNP has recently been studied (16,17).

There is no precise cut-off value in the literature for BNP levels from which it predicts clinical outcomes or cardiovascular mortality in STEMI patients, most of the studies using BNP as a dichotomous result at 80pg/ml (12,18-20).

□

OBJECTIVES

The aim of this study was to assess the predictive value of BNP serum levels for left ventricular function assessed by echocardiography in STEMI patients undergoing revascularization. □

MATERIAL AND METHODS

Study Population and treatment

From January 2005 until July 2006 we prospectively studied a cohort of 88 consecutive patients, with mean age 51.6 years, 88.6% males (Table 1) hospitalized in our clinic for STEMI in Killip class I (50% anterior infarction), who underwent reperfusion therapy within a mean time from symptoms onset of 3.82 hours (range 1-12 hours).

Thrombolysis was used in 87.5% of cases (30.3% streptokinase, 69.7% tissue plasminogen activator) and primary percutaneous coronary intervention (PTCA) in 11.5% of cases. Successful reperfusion (R) assessed non-invasively by classical criteria, mainly by ST-segment resolution, was obtained in 88.6% of patients, of whom 19.3% had reperfusion injury (RI) defined by acute heart failure and episodes of arrhythmias requiring intervention. In the remaining 11.4% there was lack of reperfusion (NR) (Table 2).

Serum BNP levels were measured on admission (BNP0), at 24h (BNP24) and at 30 days (BNP30) after reperfusion. Detailed echocardiography was performed at baseline, at 24 hours after reperfusion, on discharge (at 7 – 10 days) and at follow-up at 1 month. Left ventricular (LV) systolic and diastolic dysfunction were defined by LVEF < 45% and E/A ratio respectively (figure 1). □

Statistics

Data analysis was performed using Statistical Package for Social Sciences (SPSS 15.0) software (SPSS Inc., Chicago, IL, USA), at a significance level of $p \leq 0.05$.

Kolmogorov-Smirnov test was used to analyze continuous data distribution, according to which appropriate tests were further used in analysis: independent samples t-test or Mann-Whitney U test for differences between means of 2 independent groups, and paired-samples t-test or Wilcoxon test for differences between

Variable		p value*
Sex		
• Male	88.6%	p = 0.0001
• Female	11.4%	
Age (years)	51.6 (26-78)	
BMI (Kg/m ²)	27.58 (19.81 – 39.34)	
Smoker status		
• Non-smoker	20.5%	p = 0.0001
• Smoker	79.5%	
Diabetes		
• Absent	87.5%	p = 0.0001
• Present	12.5%	
Dyslipidemia		
• Absent	47.7%	p = 0.670
• Present	52.3%	
Hypertension		
• Absent	51.1%	p = 0.831
• Present	48.9%	
Late angina		
• Absent	52.3%	p = 0.0001
• Present	47.7%	
AMI location		
• Anterior	50%	p = 1
• Inferior	50%	

TABLE 1. Demographic and clinical features of studied patients

Data are presented as a percentage for categorical variables and as mean value (range) for continuous variables. BMI = body mass index; * = chi square test

Variable		p value*
TTT (hours)	3.82 (1 – 12)	
Revascularization		
• Thrombolysis	87.5%	p = 0.0001
• PPTCA	12.5%	
Thrombolitics		
• AT	25%	p = 0.713
• RE	21%	
• SK	30.3%	
• TE	23.7%	
RTR		
• NR	11.4%	p = 0.0001
• R	69.3%	
• RI	19.3%	

TABLE 2. Reperfusion therapy

Data are presented as a percentage for categorical variables and as mean value (range) for continuous variables; TTT = time from symptom onset to therapy; RTR = reperfusion therapy results; NR = no reperfusion; R = reperfusion; RI = reperfusion injury; PPTCA = primary percutaneous coronary angioplasty; AT = alteplase; RE = reteplase; SK = streptokinase; TE = tenecteplase; * = chi square test

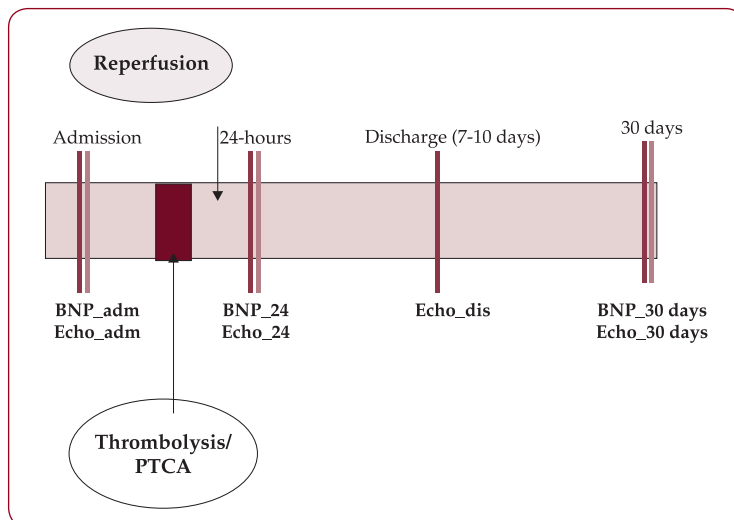


FIGURE 1. Study design

BNP = B-type Natriuretic peptide; 0 = on admission; 24 = at 24 hours after revascularization, 30 = at 30 days after revascularization; PTCA = percutaneous coronary angioplasty; Echo = echocardiography; dis = discharge

means of 2 related groups. Chi-square test was used to analyze differences between categorical data.

Person's or Spearman's correlation coefficients were calculated in order to test the association between variables.

The predictive value of BNP for detecting and systolic / diastolic left ventricular dysfunction was assessed using receiver-operating characteristics (ROC) analysis, identifying the cut point value that maximizes sensitivity and specificity. □

RESULTS

BNP levels and systolic/diastolic LV dysfunction

During hospitalization, 51.1% of all patients presented systolic LV dysfunction (SLVD-H: defined by LVEF < 45% on at least one of three measurements: on admission, at 24 hours after reperfusion therapy and on discharge) and 61.4% of all patients presented diastolic LV dysfunction (DLVD-H: defined by E/A < 1 or E/A > 2 on at least one of three measurements: on admission, at 24 hours after reperfusion therapy and on discharge).

At follow-up (30 days after reperfusion therapy) there was a significant reduction in proportion of patients with both systolic and diastolic LV dysfunction [28.4% SLVD-30 vs. 51.1% SLVD-H; p = 0.0001; and respectively 43.2% DLVD-30 vs. 61.4% DLVD-H; p = 0.0001] (figure 2).

Systolic left ventricular dysfunction during hospitalization was found significantly more frequent in patients with anterior AMI comparing to those with inferior location [76.2% vs. 33.3%; p = 0.0001] while at 30 after revascularization, the proportion of cases with systolic left ventricular dysfunction was statistically similar in both groups [39.5% vs. 21.1%; p = 0.072].

The proportion of cases with diastolic left ventricular dysfunction was statistically similar for both anterior and inferior AMI patients during hospitalization [88.9% vs. 78.6%; p = 0.259] while, at follow, up it was significantly higher in anterior AMI patients [72.2% vs. 44.4%; p = 0.026] (table 3).

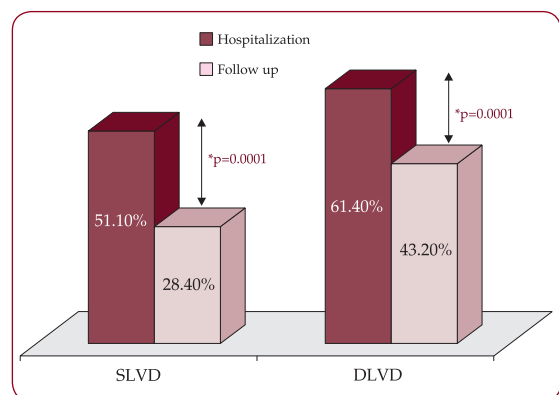


FIGURE 2. LV dysfunction during hospitalization and at follow up

SLVD = systolic left ventricular dysfunction; DLVD-H = diastolic left ventricular dysfunction

	ANT. AMI	INF. AMI	p value
SLVD-H (%)	76.2	33.3	p = 0.0001*
DLVD-H (%)	88.9	78.6	p = 0.259*
SLVD-30 (%)	39.5	21.1	p = 0.072*
DLVD-30 (%)	72.2	44.4	p = 0.026*

TABLE 3. Systolic and diastolic left ventricular dysfunction by AMI location

Data are presented as a percentage; SLVD-H = systolic left ventricular dysfunction during hospitalization; DLVD-H = diastolic left ventricular dysfunction during hospitalization; SLVD-30 = systolic left ventricular dysfunction at 30 days after revascularization; DLVD-30 = diastolic left ventricular dysfunction at 30 days after revascularization; ANT.AMI = anterior acute myocardial infarction; INF. AMI = inferior acute myocardial infarction; * = chi square test

Both on admission and at 24 hours after reperfusion, patients with anterior AMI had the highest BNP levels [BNP0: 84.33 pg/ml vs. 34.83 ng/ml; p = 0.033; BNP24: 259.32 pg/ml vs. 178.86 pg/ml; p = 0.044], while at 30 days after revascularization therapy BNP levels were similar in both groups [BNP30: 197.49 pg/ml vs. 188.3 pg/ml; p = 0.857] (table 4).

BNP dynamics (pg/ml)	ANT AMI	INF AMI	p value
BNP0	84.33 (4-589)	34.83 (4-157)	p = 0.033*
BNP24	259.32 (9.1-946)	178.86 (7.9-690)	p = 0.044*
BNP30	197.49 (10.2-861)	188.30 (12.9-1380)	p = 0.857*

TABLE 4. Differences in BNP levels in patients with anterior or inferior AMI

Data are presented as mean value (range); BNP = B-type Natriuretic peptide; 0 = on admission; 24 = at 24 hours after revascularization, 30 = at 30 days after revascularization; ANT.AMI = anterior acute myocardial infarction; INF. AMI = inferior acute myocardial infarction; * = independent samples t test

Starting from statistically similar BNP levels on admission, patients whom presented systolic LV dysfunction during hospitalization and at follow up, had significantly higher BNP24 and BNP30 levels compared to those without systolic LV dysfunction. [SLVD on admission absent vs. present: BNP0: 50.45 pg/ml vs. 70.77 pg/ml; p = 0.599; BNP24: 147.03 pg/ml vs. 282.46 pg/ml; p = 0.001; BNP30: 130.47 pg/ml vs. 246.47 pg/ml; p = 0.007; SLVD at follow up absent vs. present: BNP0: 56.04 pg/ml vs. 70.99 pg/ml; p = 0.906; BNP24: 175.90 pg/ml vs. 305.76 pg/ml; p = 0.021; BNP30: 147.56 pg/ml vs. 298.92 pg/ml; p = 0.001]. (figure 3).

In anterior AMI patients there was a direct association of medium strength between BNP levels at 24 hours and at 30 days after the reperfusion therapy and systolic LV dysfunction during hospitalization [BNP0 – SLVD-H: rs = 0.396; rs2 = 0.156; p = 0.010; BNP30– SLVD: rs = 0.317; rs2 = 0.100 p = 0.044]. There were no statistic significant association between BNP levels and dyastolic LV dysfunction in this group of patients.

In inferior AMI patients there was a direct association of medium strength between BNP levels at 30 days after the reperfusion therapy and both systolic LV dysfunction during hospitalization and diastolic LV dysfunction at follow up [BNP30– SLVD-H: rs = 0.332; rs2 = 0.110 p = 0.048; BNP30– DLVD-30: rs = 0.383; rs2 = 0.146 p = 0.049]. There were no statistic significant association between BNP0 and BNP24 levels and systolic or diastolic LV dys-

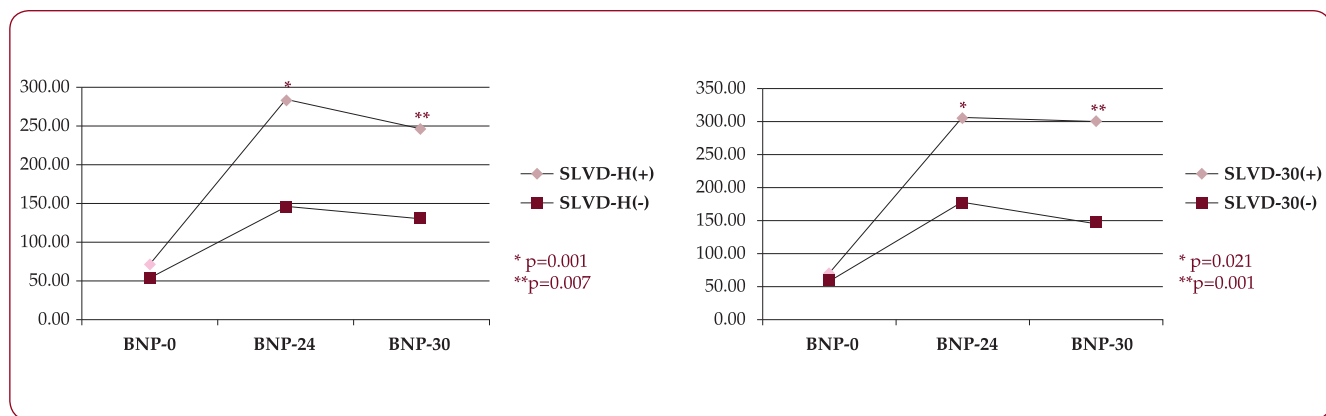


FIGURE 3. BNP levels and LV dysfunction

BNP = B-type Natriuretic peptide; 0 = on admission; 24 = at 24 hours after revascularization, 30 = at 30 days after revascularization; SLVD-H = systolic left ventricular dysfunction during hospitalization; SLVD-30 = systolic left ventricular dysfunction at 30 days after revascularization; (+) = with; (-) = without

function during hospitalization in this group of patients.

ROC curve analysis showed that BNP measurements on admission and at 24 hours after revascularization have no predictive value for diastolic LV dysfunction neither in anterior nor in inferior AMI patients (figure 4). Also these measurements have no predictive value for systolic LV dysfunction in inferior AMI patients (figure 5 (b)). Only BNP levels at 24 hours after revascularization can predict systolic LV dysfunction in anterior AMI patients with a 90.3% sensitivity and a 60% false positive rate (1-specificity) at a cutt off value of 90pg/ml (figure 5 (a)). □

DISCUSSION

In this study we have demonstrated that the early BNP measurement provides important information regarding systolic LV dysfunction in STEMI with anterior location patients undergoing revascularization.

Elevated BNP after AMI identifies patients at risk of adverse left ventricular remodeling, chronic left ventricular dysfunction and congestive heart failure (23).

It is well known that BNP levels are correlated with age, renal function, intracardiac pressures and ejection fraction (17). The majority of patients enrolled in this study were of mas-

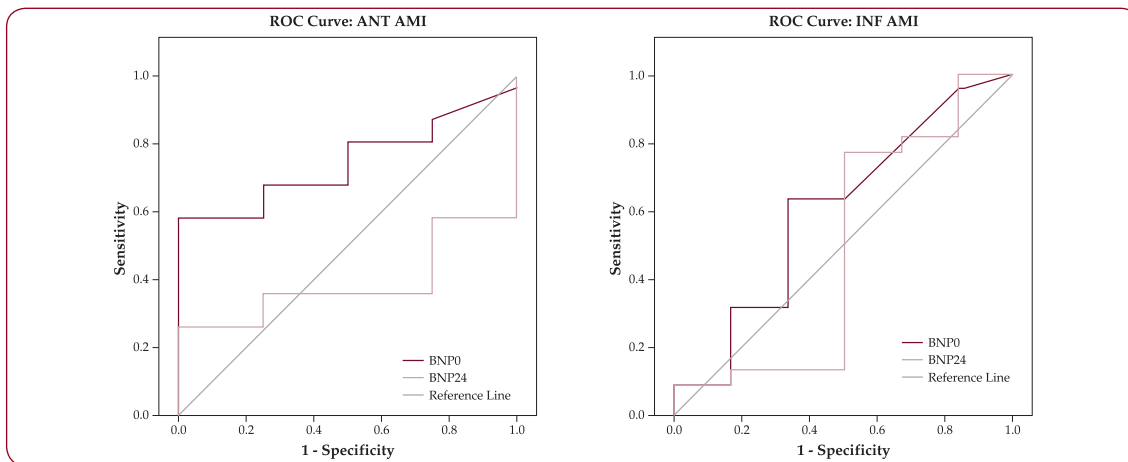


FIGURE 4. ROC curve for BNP predicting diastolic LV dysfunction

Receiver operating characteristic (ROC) curve analysis for B-type Natriuretic peptide (BNP) levels on admission (0) and at 24 hours (24) after revascularization therapy as predictor for diastolic LV dysfunction; (a) ANT. AMI = anterior acute myocardial infarction; (b) INF AMI = inferior acute myocardial infarction

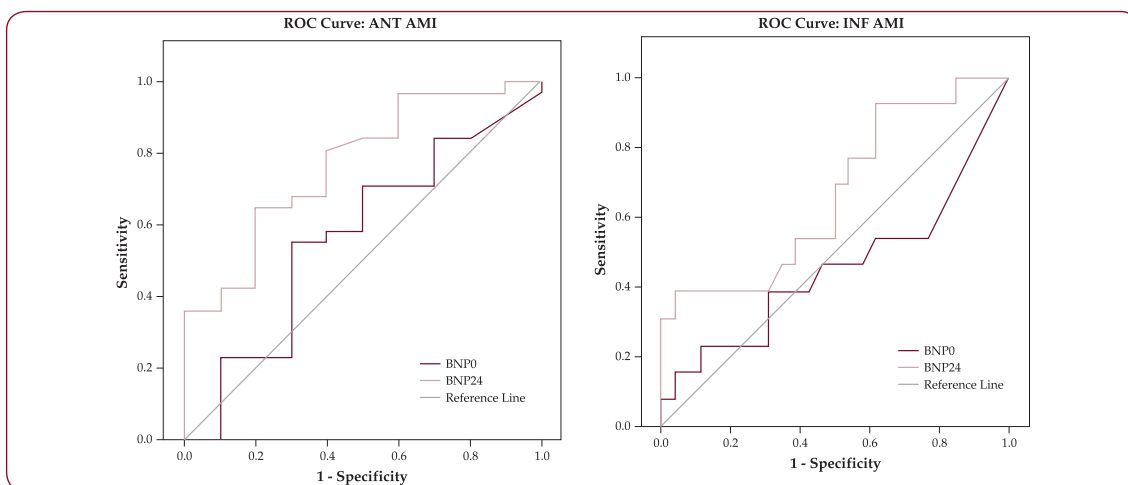


FIGURE 5. ROC curve for BNP predicting systolic LV dysfunction

Receiver operating characteristic (ROC) curve analysis for B-type Natriuretic peptide (BNP) levels on admission (0) and at 24 hours (24) after revascularization therapy as predictor for systolic LV dysfunction; (a) ANT AMI = anterior acute myocardial infarction; (b) INF AMI = inferior acute myocardial infarction

culin gender and of rather young age. Renal impairment defined by creatinine clearance ≤ 30 ml/min was used as an exclusion criterion. More than that, we've used Killip class I STEMI as a inclusion criterion in order to ensure that at baseline patients were similar regarding LV filling pressure due to prior disease and the consequent BNP levels dynamics could be interpreted as a consequence of LV filling pressure variation secondary to the reperfusion outcome. Thus we've minimalised the factors that could bias our data.

This study provides support for the use of BNP as a screening tool for systolic LV dysfunction in anterior AMI patients at a threshold of 90 pg/ml. This threshold is very similar to that established for the diagnostic of chronic heart failure (100 pg/ml) in a recent prospective study (24). Therefore, routine treatment, even without clinical LV dysfunction, with after load reducing agents or other agents that may improve infarct healing or ventricular remodeling after AMI may be particularly beneficial in STEMI patients with early elevated BNP serum levels.

At this moment there is no management strategy based on early elevated BNP levels for STEMI patients. Additional studies are needed to identify novel therapies that may reduce the

risk associated with increased BNP levels in STEMI patients.

Limitation to this study should be considered. First, this study had a relatively small number of patients, so data should be interpreted with caution. Second, the lack of LV function data is an objective limitation of our study.

CONCLUSIONS

1. Early measurement of BNP levels may allow early prediction of anterior AMI patients at risk of developing systolic LV dysfunction after revascularization therapy.
2. An elevated plasma concentration of BNP (>90 pg/ml) at 24 hours after revascularization in anterior AMI patients predicts systolic LV dysfunction with 90.3% sensitivity and a 60% false positive rate. \square

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