Value of brain natriuretic peptide after acute myocardial infarction

Akut miyokard infarktüsü sonrası beyin natriüretik peptid'in değeri

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ABSTRACT

Objective: Brain natriuretic peptide (BNP) is secreted predominantly from the ventricles in response to increased wall stress, which is known to be one of the major forces driving left ventricular (LV) remodeling. In this prospective study, we evaluated value of BNP levels in acute myocardial infarction (MI) patients for the prediction of heart failure during one year of follow-up.

Methods: Seventy-four patients with a first ST-elevation MI were examined prospectively after 5 days and 1 month with echocardiography and blood samples for BNP were obtained. Clinical events were recorded during 12 months of follow-up. Multivariate linear regression analysis was used to analyze the value of different baseline characteristics as independent predictors of LV ejection fraction (LVEF) ≤ 40% and clinical heart failure. Diagnostic ability of BNP to detect LVEF ≤ 40% and heart failure was evaluated with receiver operating characteristic (ROC) curves.

Results: Brain natriuretic peptide levels were higher in patients developing symptomatic heart failure during follow up irrespective of presence of LVEF ≤40% (68.9±52.5 vs 21.4±18.4, p=0.003, for baseline BNP and 79.3±35.8 pg/ml vs. 22.9±15.8 pg/ml for one month BNP, p<0.001). Regression analysis including pain duration, peak creatine kinase-MB levels, MI localization, baseline BNP levels and baseline LV volumes yielded that baseline BNP was the most powerful predictor of one-year LVEF ≤40% (Beta: 0.376, p=0.004). Multivariate analyses, testing for independent predictive information of pain duration, peak creatine kinase-MB, MI localization, thrombolytic therapy or primary percutaneous intervention, fifth day and one month LV volumes, LVEF and BNP levels, for development of clinical heart failure, showed that one month BNP was the single significant predictor (Beta: 0.675, p<0.001). There was a negative correlation between BNP levels and LVEF (r=-0.599, p<0.001, for baseline BNP level). Higher BNP levels were associated with greater increase in LV end-systolic (r= 0.531, p< 0.001) and end-diastolic volumes (r= 0.385, p= 0.001) during one year of follow-up. A baseline BNP level of >39 pg/ml identified LVEF ≤ 40% at one year with a sensitivity of 72.7% and specificity of 91.9% (OR=30.4, 95% CI, 6.1-152.3, p<0.001, AUC=0.852). A BNP level >39 pg/ml also increased the risk of clinical heart failure (for baseline BNP sensitivity: 60.0%, specificity 89.1%, OR=12.2; 95% CI, 2.7-54.1, p=0.001 and for one month BNP sensitivity: 80.0%, specificity 85.9%, OR=24.4; 95% CI, 4.5-134.1, p<0.001).

Conclusions: High level of BNP is a powerful marker of LV systolic dysfunction and poor prognosis after MI. Increased BNP levels are associated with progressive ventricular dilatation and development of clinical heart failure. *(Anadolu Kardiyol Derg 2008; 8: 182-7)*

Key words: Brain natriuretic peptide, myocardial infarction, heart failure, ROC analysis, predictive value of tests

ÖZET

Amaç: Beyin natriüretik peptid (BNP) sol ventrikül (LV) yeniden şekillenmesinde temel bir itici güç olduğu bilinen duvar gerilimi artışına yanıt olarak daha çok ventriküllerden salınır. Dolayısıyla, boşluklarda genişleme olmadan önce riski yüksek olan hastaları tespit etmek mümkün olabilir. Bu prospektif çalışmada akut miyokard infarktüsü (Mİ) hastalarında BNP düzeylerinin bir yıllık takip sürecinde kalp yetersizliği gelişmesini öngörme değerini araştırdık.

Yöntemler: İlk kez ST-yükselmeli Mİ geçiren yetmiş dört hasta prospektif olarak beş gün ve bir ay sonra ekokardiyografi ile değerlendirildi ve BNP için kan örnekleri alındı. On iki aylık takip süresinde klinik olaylar kaydedildi. Bazal değişkenlerin sol ventrikül ejeksiyon fraksiyonu (SVEF) ≤%40 ve klinik kalp yetersizliğini bağımsız olarak öngörebilme yetilerini değerlendirmek için çoklu regresyon analizi kullanıldı. Beyin natriüretik peptidin SVEF ≤%40 ve kalp yetersizliğini saptayabilme kabiliyeti ROC analizi ile değerlendirildi.

Bulgular: Beyin natriüretik peptid düzeyleri klinik kalp yetersizliği gelişen hastalarda, SVEF ≤%40 olsun veya olmasın, daha yüksekti (bazal BNP: 68.9±52.5 vs 21.4±18.4 pg/ml, p=0.003, birinci ay BNP: 79.3±35.8 vs. 22.9±15.8 pg/ml, p<0.001). Ağrı süresi, zirve kreatin kinaz MB fraksiyonu (CK-MB) düzeyleri, Mİ yerleşimi, bazal BNP düzeyleri ile SV hacimlerini içeren regresyon analizinde bazal BNP düzeyi birinci yıl SVEF ≤%40'ı öngören en güçlü parametre idi (Beta: 0.376, p=0.004). Ağrı süresi, zirve CK-MB düzeyleri, Mİ yerleşimi, trombolitik veya primer perkütan girişim ile tedavi ile beşinci gün ve birinci ay SV hacimleri, EF ve BNP düzeylerini içeren regresyon analizinde klinik kalp yetersizliğini öngören tek anlamlı parametre birinci ay BNP düzeyi idi (Beta: 0.675, p<0.001). Beyin natriüretik peptid düzeyleri ile sol ventrikül ejeksiyon fraksiyonu arasında negatif bir ilişki saptandı (r=-0.599, p<0.001, bazal BNP düzeyi için). Bir yıllık takip süresinde daha yüksek BNP değerlerinin SV sistol sonu (r= 0.531, p<0.001) ve diyastol sonu (r= 0.385, p= 0.001) hacimlerinde daha fazla artışla ilişkili olduğu gözlendi. 39 pg/ml BNP sınır değeri %72.7 duyarlılık ve %91.9 özgüllük ile birinci yıl SVEF ≤40'ı öngörebilmekteydi (OR=30.4, %95 GA, 6.1 -152.3, p<0.001, AUC=0.852) ve 39 pg/ml BNP sınır değeri klinik kalp yetersizliği riskini de artırmaktaydı (bazal BNP için duyarlılık: %60.0, özgüllük %89.1, OR=12.2; %95 GA, 2.7-54.1, p=0.001; birinci ay BNP için duyarlılık: %80.0, özgüllük: %85.9, OR=24.4; %95 GA, 4.5-134.1, p<0.001).

Sonuç: Yüksek BNP düzeyleri LV sistolik disfonksiyonunun ve Mİ sonrası kötü prognozun önemli bir belirtecidir. Yüksek BNP düzeyleri ventrikülde ilerleyici genişleme ve klinik kalp yetersizliği oluşumuyla ilişkilidir. *(Anadolu Kardiyol Derg 2008; 8: 182-7)*

Anahtar kelimeler: Beyin natriüretik peptid, miyokard infarktüsü, kalp yetersizliği, ROC analizi, testlerin prediktif değeri

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Introduction

Brain natriuretic peptide (BNP) is secreted predominantly from the ventricles, and its plasma levels have been shown to be increased after myocardial infarction (MI) and associated with left ventricular (LV) systolic dysfunction (1). The strongest markers of prognosis after MI are degree of LV systolic dysfunction, severity of coronary artery disease and presence of heart failure (2). Left ventricular remodeling is a detrimental complication of MI characterized by dilatation of heart chambers, change in chamber geometry and progressive deterioration of LV function. Remodeling is directly related with development of heart failure and poor prognosis (2-5). Therefore, it's important to detect patients at high risk of LV remodeling at the earlier stages. The parameters used in the detection of remodeling are heart size, shape and mass, ejection fraction, end-diastolic and end-systolic volumes and peak force of contraction. Use of echocardiography is accepted as standard practice in the identification of LV systolic dysfunction (2). Brain natriuretic peptide plasma concentrations are increased in patients with heart failure (6). Several studies suggest that BNP is associated with development of heart failure and mortality after MI (7-9). It has been demonstared that BNP was associated with LV systolic dysfunction and progressive LV remodeling after MI (10-12). In this prospective study, we evaluated value of BNP levels in acute MI patients for the prediction of heart failure during one year of follow-up.

Methods

Seventy-four patients with a first and ST-elevation MI were prospectively recruited from Istanbul University Institute of Cardiology. Inclusion criteria were a diagnosis of chest pain of at least 30 minutes duration and electrocardiographic ST-segment elevation of 2 mV or more in at least two contiguous precordial leads or 1 mV or more in two contiguous extremity leads and increase in creatinine kinase-MB (CKMB) levels three times or more.

Patients with renal failure (creatinine >2 mg/dL), severe heart failure (> Killip II), hypertension with marked LV hypertrophy at echocardiography (interventricular septum thickness >1.2 cm, posterior wall thickness >1.2 cm on M-mode), previous MI, cardiomyopathy, chronic atrial fibrillation, severe pulmonary hypertension and significant valvular disease were excluded.

After the prospective follow-up patients were categorized into two groups according to development of heart failure. The BNP levels defined in literature vary depending on the assay procedure used and the study population. To achieve reference intervals for BNP levels blood samples were obtained from 31 healthy control subjects matched for age of study group and having no history of hypertension, diabetes, structural heart disorder or any other systemic disorder and having normal echocardiographic findings. All patients gave written informed consent to the study, and the study was approved by the Istanbul University Cerrahpaşa Medical School ethical committee.

Creatinine kinase-MB levels were measured on admission and after 6, 12, 24 and 48 hours. Echocardiographic examination was performed 5 days, 1 month and 1 year after ischemic insult. All studies were performed using an Acuson C Sequoia 250 instrument and a 3.5 MHz phased transducer. The subjects were in left lateral recumbent position. Left ventricular ejection fraction (LVEF) was calculated by modified Simpson rule with acquisition of LV end-diastolic (EDV) and end-systolic (ESV) volumes at apical two- and four-chamber views with the mean of at least three measurements.

Blood samples for BNP were obtained at baseline (fifth day) and 1 month after MI, into EDTA (Na) tubes. Samples were immediately centrifuged and aspirated plasma was transferred into plastic test tubes that were stored at -70 °C until analysis. Plasma BNP concentrations were determined by use of a specific competitive radioimmunoassay kit (Phoenix Pharmaceutical) (range 1-128 pg/tube).

Statistical analysis

All tests were performed using SPSS for Windows, version 10.0 software (Chicago, IL, USA). Difference between independent groups was assessed by Mann Whitney U test and, in the case of dichotomous variables by Chi-square test as appropriate. Pearson correlation analyses were used to assess the association of BNP levels and LV measures. Multivariate linear regression analysis was used to analyze the value of pain duration, peak CK-MB levels, MI localization, baseline BNP levels and baseline LV volumes as independent predictors of LVEF ≤40% at one year and to assess independent predictive information of peak CKMB, MI localization, thrombolytic therapy or primary percutaneous coronary intervention (PCI), baseline and one month LV volumes, EF and BNP levels for development of clinical heart failure. Ability of BNP to detect LVEF ≤40% and clinical heart failure was evaluated using receiver operating characteristic (ROC) curves and area under curves (AUC), confidence intervals (CI) and p values were calculated. All results were considered statistically significant at the level of $p \leq 0.05$.

Results

Mean BNP levels were significantly higher in patients than in the healthy control group (27.8±29.0 vs. 17.3±8.1 pg/ml, p= 0.001). When only the patients with LVEF >40% were compared with healthy group, significance was no longer present (21.9±21.9 vs. 17.3±8.1 pg/ml, p= 0.21). One patient died and ten patients developed congestive heart failure during follow-up. Two patients were classified as having Killip class III and others as Killip class II. Patient characteristics, categorized according to development of heart failure, are given in Table 1. Frequency of anterior MI (p=0.036), pain duration (p=0.011) and peak CKMB (p=0.006) levels were higher in clinical heart failure patients (Table 1). Brain natriuretic peptide levels were higher (p=0.003 for basal BNP and p<0.001 for one month BNP) in patients developing symptomatic heart failure during follow-up irrespective of presence of LVEF ≤40% (Table 1 and 2). Also, BNP levels were higher (p<0.05) in patients with LVEF ≤40% than in patients with LVEF>40% whether clinical heart failure present or not (Table 2).

There was a significant correlation between baseline BNP levels and peak CKMB levels (271.8±210.1 IU/L; r=0.539; p<0.001). The BNP levels were significantly correlated with LVEF and LV volumes (Table 3). In patients developing heart failure, BNP levels and LV volumes were significantly higher and LVEF was less than in those without heart failure (Table 4, Fig. 1). One-year change in LV volumes was calculated with subtraction of one year LV volumes from baseline LV volumes. A significant correlation between BNP levels and LV dilatation was detected (EDV change: r=0.385, p=0.001; ESV change: r=0.531, p<0.001).

Regression analysis including pain duration, peak CK-MB levels, MI localization, baseline BNP levels and baseline LV volumes yielded that baseline BNP (Beta: 0.376, p=0.004) and ESV (Beta: 0.312, p=0.016) were the significant predictors of one-year LVEF ≤40% (Table 5). Multivariate analyses, testing for independent predictive information of pain duration, peak CKMB, MI localization, thrombolytic therapy or primary PCI, fifth day and one-month LV volumes, EF and BNP levels, for development of clinical heart failure, showed that one month BNP was the only significant predictor (Beta: 0.675, p<0.001) (Table 6).

Table 1. Patients characteristics

Variables	Total (n=74)	Patients developing heart failure (n=10)	Patients not developing heart failure (n=64)	p
Age, years	48.9±9.4	50.4±9.2	48.8±8.4	NS
Male, n (%)	60 (81.1)	9 (90)	51 (79.7)	NS
Body mass index, kg/m²	26.4±2.6 26.3 (20.3-32.6)	27.6±2.8 27.5 (23.2-31.2)	26.3±2.6 26.3 (20.3-32.6)	NS
Smoking, n (%)	52 (70.3)	7 (70)	45 (70.3)	NS
Hypertension, n (%)	27 (36.5)	4 (40)	23 (35.9)	NS
Diabetes, n (%)	11 (14.9)	1 (10)	10 (15.6)	NS
Hyperlipidemia, n (%)	25 (33.8)	6 (60)	19 (29.7)	NS
Family history of CAD, n (%)	8 (10.8)	1 (10)	7 (10.9)	NS
Obesity (BMI > 30 kg/m²), n (%)	8 (10.8)	2 (20)	6 (9.3)	NS
Thrombolytic therapy, n (%)	52 (70.3)	8 (80)	44 (68.7)	NS
Primary or rescue PCI, n (%)	24 (32.4)	4 (40)	20 (31.2)	NS
Anterior MI, n (%)	40 (54.1)	9 (90)	32 (50.0)	0.036
Pain duration , min	237.9±185.0 180 (30-840)	363.0±214.7 300 (120-840)	220.3±175.2 180 (30-840)	0.011
Peak-CKMB, IU/L	271.8±210.1 215 (39.0-1265)	388.6±252.4 420 (145-1100)	271.7±227.3 191.5 (39.0-1265)	0.006
Beta-blocker, n (%)	56 (75.8)	7 (70)	49 (76.5)	NS
ACE inhibitors, n (%)	59 (79.8)	8 (80)	51 (79.7)	NS
BNP fifth day , pg/ml	27.8±29.9 18.0 (1.3-128.0)	68.9±52.5 49.5 (9.9-128.0)	21.4±18.4 16.0 (1.3-128.0)	0.003
BNP one month , pg/ml	30.5±27.4 20.5 (1.0-128.0)	79.3±35.8 78.5 (37.0-128.0)	22.9±15.8 18.0 (1.0-75.0)	<0.001

Data are represented as Mean±SD, Median (Minimum-Maximum) values and proportion/percentage

Mann Whitney U test and Chi-square test

ACE- angiotensin converting enzyme, BMI- body mass index, BNP- brain natriuretic peptide, CAD- coronary artery disease, CKMB- creatine kinase MB fraction, MI- myocardial infarction, NS- not significant, PCI- percutaneous coronary intervention

Table 2. Comparison of BNP levels according to development of clinical heart failure and LVEF

	Patient group				Control group	
Clinical heart failure	EF≤%40		EF>%40			
	BNP, pg/ml	n	BNP, pg/ml	n	BNP, pg/ml	n
Yes	81.7±36.9*	6	75.7±39.2+	4	17.3±8.1	31
No	47.7±6.5++	3	21.7±15.1	61		

Data are represented as Mean±SD, values

Mann Whitney U test

* p<0.05, patients having LVEF≤%40 with clinical heart failure vs. patients having LVEF≤%40 not developing heart failure

+ p<0.05, patients having LVEF>%40 with clinical heart failure vs. patients having LVEF>%40 not developing heart failure and control group

+ + patients not developing clinical heart failure with LVEF≤%40 vs. patients not developing clinical heart failure with LVEF>%40 and control group

BNP - brain natriuretic peptide, EF- ejection fraction

Receiver operating curve analysis revealed that a baseline BNP level of >39 pg/ml identified LVEF ≤40% at first month with a sensitivity of 61.5% and a specificity of 92.3% (AUC=0.892, 95% CI: 0.806-0.978, p<0.001). A baseline BNP level above 39 pg/ml increased the risk of having one month LVEF ≤40% by 96 times (Odds ratio [OR]) (95% CI, 9.9-929.4, p<0.001) and one-year LVEF ≤40% by 30.4 times with a sensitivity of 72.7% and specificity of 91.9% (95% CI, 6.1 -152.3, p<0.001). Odds ratio of one-month BNP for one-year LVEF ≤40% was 49.8 (95% CI, 5.5-446.9, p<0.001) (Fig. 2). A BNP level >39 pg/ml also increased the risk of clinical heart failure (for baseline BNP sensitivity: 60.0%, specificity 89.1%, OR=12.2; 95% CI, 2.7-54.1, p=0.001 and for one-month BNP sensitivity: 80.0%, specificity 85.9%, OR=24.4; 95% CI, 4.5-134.1, p<0.001) (Fig. 3).

Table 3. Correlation of BNP with left ventricular volumes and ejection fraction

	Baseline BNP		One-month BNP	
	r	p	r	p
Baseline LVEF, %	-0.599	<0.001	-0.412	<0.001
One -month LVEF, %	-0.578	<0.001	-0.552	<0.001
One-year LVEF, %	-0.584	<0.001	-0.594	<0.001
Baseline EDV, cm^3	0.274	0.018	0.435	<0.001
One-month EDV, cm^3	0.260	0.025	0.429	<0.001
One-year EDV, cm^3	0.303	0.009	0.466	<0.001
Baseline ESV, cm^3	0.471	<0.001	0.516	<0.001
One-month ESV, cm^3	0.474	<0.001	0.548	<0.001
One-year ESV, cm^3	0.519	<0.001	0.612	<0.001

Pearson correlation analysis
BNP- brain natriuretic peptide, EDV- end- diastolic volume, EF- ejection fraction, ESV- end-systolic volume, LV- left ventricle

Table 4. BNP levels, LVEF and LV volumes in patients with and without heart failure development

Variables	Heart failure		p
	yes (n= 10)	no (n=64)	
Baseline BNP, pg/ml	68.9±52.5 49.5 (9.9-128.0)	21.4±18.4 16.0 (1.3-128.0)	0.003
1 month BNP, pg/ml	79.3±35.8 78.5 (37.0-128.0)	22.9±15.8 18.0 (1.0-75.0)	<0.001
Baseline LVEF, %	40.3±7.4 41 (30-54)	48.7±5.2 49 (38-61)	0.001
1 month LVEF, %	38.1±7.3 38 (27-49)	50.7±5.5 51 (38-65)	<0.001
Baseline EDV, cm^3	123.2±30.2 118.0 (86.7-179.0)	102.5±24.5 97.5 (53.0-192.0)	0.038
1 month EDV, cm^3	126.7±26.3 129.0 (97.0-169.0)	107.7±23.6 106 (59.1-181.0)	0.003
Baseline ESV, cm^3	73.9±22.2 69.0 (46.0-123.0)	53.1±14.8 51.5 (22.0-87.0)	0.004
1 month ESV, cm^3	80.2±26.6 77 (46.0-123.0)	54.1±14.3 51.5 (23.0-87.0)	0.002

Data are represented as Mean±SD, Median (Minimum-Maximum) values
Mann Whitney U test
BNP- brain natriuretic peptide, EDV- end-diastolic volume, EF- ejection fraction, ESV- end-systolic volume, LV- left ventricle

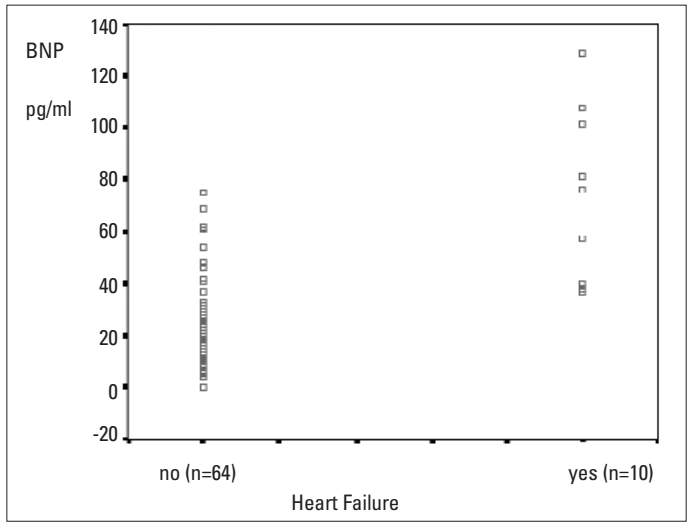

Figure 1. Distribution of baseline brain natriuretic peptide (BNP) levels in respect to development of clinical heart failure

Table 5. Predictive value of baseline variables for one-year LVEF

	Beta	p
BNP, pg/ml	0.376	0.004
LV ESV, cm^3	0.312	0.016
LV EDV, cm^3	0.024	0.836
Pain duration, minutes	0.107	0.318
Anterior MI	0.063	0.554
Peak CK-MB, IU/L	0.105	0.392

Multivariate regression analysis
BNP - brain natriuretic peptide, CKMB- creatine kinase MB fraction, EDV- end- diastolic volume, EF- ejection fraction, ESV- end-systolic volume, LV- left ventricle, MI- myocardial infarction

Table 6. Predictive value of BNP levels, clinical and echocardiographic variables for prediction of heart failure

	Beta	p
BNP one month, pg/ml	0.675	<0.001
BNP 5 day, pg/ml	0.001	0.993
EDV one month, cm^3	0.195	0.548
EDV 5 day, cm^3	0.116	0.539
ESV one month, cm^3	0.164	0.715
ESV 5 day, cm^3	0.043	0.694
LVEF one month, %	0.211	0.416
LVEF 5 day, %	0.078	0.583
Pain duration, minutes	0.069	0.474
Anterior MI	0.034	0.720
Peak CK-MB, IU/L	0.022	0.843
Thrombolytic therapy	0.078	0.486
Primary PCI	0.069	0.496

Multivariate regression analysis
BNP- brain natriuretic peptide, CKMB- creatine kinase MB fraction, EDV- end- diastolic volume, EF- ejection fraction, ESV- end-systolic volume, LV- left ventricle, MI- myocardial infarction, PCI- percutaneous coronary intervention

Discussion

In this prospective study we found that BNP levels measured at 5th day and one month after MI are significant independent predictors of clinical heart failure development, LV systolic dysfunction and progressive LV dilatation after acute MI.

There is a considerable interest in the use of BNP to detect left ventricular dysfunction. Choy et al. (10) compared quantitative and qualitative echocardiography, clinical evaluation and plasma BNP level in 75 patients who have survived the first 2 days after acute MI. They concluded that BNP may be a useful indicator for detecting LVEF <40% with a sensitivity of 84% and a specificity of 62%. However, Omland et al. (11) found that BNP levels were not significantly increased in 79 patients with LVEF <45% as determined by echocardiography 3 days after acute MI. Brain natriuretic peptide was not found to be useful in discriminating mild LV dysfunction (13). However, Groenning et al. (14) used magnetic resonance imaging as the reference method for the cardiac measurement and found that NT-proBNP was able to detect LVEF <58% with 84% sensitivity and 85% specificity. In our study, BNP level was able to detect LVEF ≤40% with a sensitivity of 92.3% and a specificity of 61.5%. Besides, there was no significant difference between BNP levels of patients with LVEF >40% and the control group.

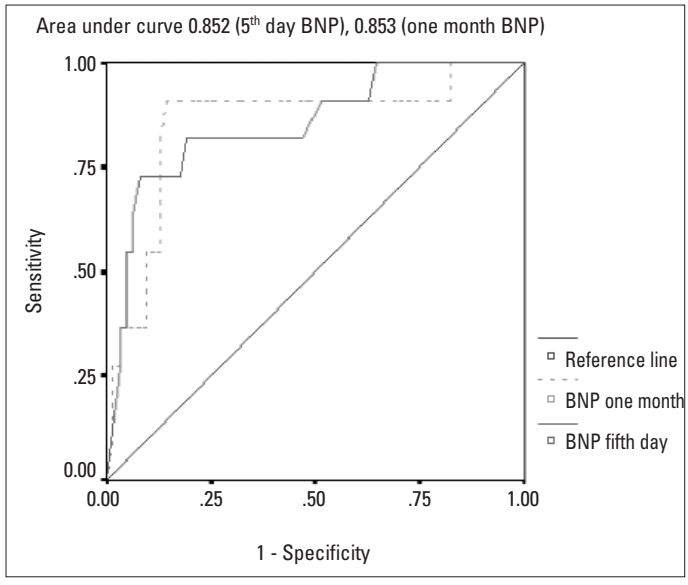

Figure 2. Receiver operating characteristic curve for ability of brain natriuretic peptide to detect left ventricular ejection fraction ≤ 40% one year after myocardial infarction

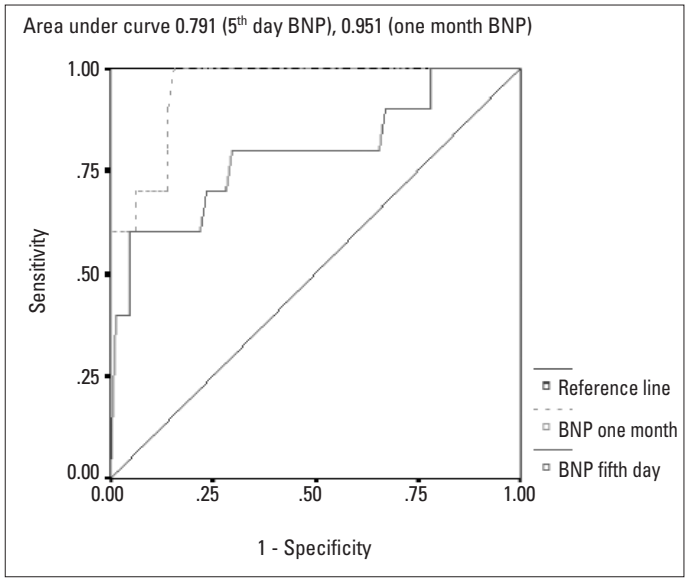

Figure 3. Receiver operating characteristic curve for ability of brain natriuretic peptide (BNP) to detect clinical heart failure within one year after myocardial infarction

It has been suggested that BNP and N-terminal pro-BNP provide additional prognostic information on long-term survival beyond that provided by LVEF (7, 11, 15-17). Since, there was only one patient died in our study, it is not possible to define the prognostic information of BNP on survival rate. Richards and coworkers (8) evaluated the prognostic utility of combining LVEF and BNP in patients with myocardial infarction. A large (n=666) cohort of patients with acute MI had concurrent measurements of BNP, amino-terminal BNP, norepinephrine, and radionuclide ejection fraction. The BNP and LVEF emerged as strong independent predictors of death, heart failure, and new myocardial infarction. More importantly, BNP and ejection fraction were complementary with increased prognostic power when combined compared to any one marker (8). Morrow et al. (7) evaluated 4266 patients with non-ST-elevation or ST-elevation acute coronary syndromes having 2 years of follow-up. Adjusting for age, sex, index event, renal function, hypertension, prior heart failure, and diabetes, elevated levels of BNP (>80 pg/ml) were associated with subsequent death or new congestive heart failure when measured at study entry (adjusted hazard ratio [HR], 2.5; 95% confidence interval [CI], 2.0-3.3). In the present study, we found BNP as the only single powerful independent predictor of symptomatic heart failure, a risk that could not be identified by LVEF. Besides, although LVEF of the died patient was preserved (baseline LVEF - 57%, one month LVEF - 52%) his BNP levels were high (baseline - 37 pg/ml, one month - 75 pg/ml).

Plasma BNP has been demonstrated to be a simple, accurate marker of progressive LV remodeling. Nilsson et al (18) followed 42 patients with a first transmural MI with magnetic resonance imaging for one year. They found that baseline NT-proBNP identified patients who later had LV dilatation with sensitivity of 89% and specificity of 68%. Smaller studies (12, 19) had also shown BNP to be predictive for LV dilatation. We found BNP to be significantly associated with LV dilatation within one year. However, baseline BNP levels did not correlate with LV volume increase within one month. The natriuretic peptide system is activated in response to adverse neurohormonal signals from the adrenergic and renin-angiotensin-aldosterone systems. Increased wall tension and stretch are also likely to be important in activation of BNP synthesis (20). These factors are known to be major forces driving LV modeling (2-5). Since we did not include patients at high risk of rapid remodeling, it may well be hypothesized that BNP may reflect small increments in LV volumes that can not be evaluated precisely by echocardiography and it is a predictor of long-term LV dilatation.

Limitations of the study

In our study, baseline examinations were performed five days after onset of MI when infarct expansion may have already taken place. However, patients at high risk of rapid LV dilatation were not included. Limited number of study participants, particularly in the group with LVEF ≤40% calls for attention in making conclusions. However, relatively high sensitivity of BNP to predict low LVEF might well be worth taking into account. The number of study patients is relatively low to define the effects of primary revascularization method and drugs used for by the patients. Larger studies with the examinations started at the onset of acute MI including high-risk patients and aiming to search drug effects would provide further information.

Conclusions

Along with previous studies, our study provides direct evidence for a relation between BNP and LV dysfunction as well as progressive LV remodeling after acute MI. We showed that BNP was a better prognostic marker than LVEF in predicting clinical heart failure.

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