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Usefulness of β-type natriuretic peptide in predicting ventricular arrhythmia in patients with left ventricular dysfunction after an acute myocardial infarction.

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Abstract

Objectives

The aim of this study was to evaluate the role of β-type natriuretic peptide (BNP), in prediction of ventricular arrythmia within 90 days after the onset of an acute myocardial infarction (MI) in patients who developed left ventricular systolic dysfunction during such period.

Background

Despite all the advances in therapeutic pharmacological measures and in spite of proven effectiveness of implantable cardioverter defibrillators in prevention and management of ventricular tachycardia, it is still a great problem and a major cause of mortality in this group of patients, so better identification of patients who could benefit from an cardioverter defibrillator and those who are unlikely to benefit would definitely improve the outcome in these patients. Moreover, proper selection would help high-risk patients get benefit from these interventions.

Patients and methods

We measured BNP in 60 consecutive patients after ST-elevation myocardial infarction and who developed left ventricular systolic dysfunction (ejection fraction<50%) (45 males, represent 75%, with mean age of 57.6±8.5 years old),3–5 days only after onset of MI.

Results

Mean age in our patients was 57.6±8.5 years (range: 35–80 years). Men constituted 73.4% (44 men) of our studied patients. We found mean NYHA of 2.9, mean Killip class of 2.8, and mean TIMI risk score of 8.2. Follow-up was done within 90 days. The number of patients who survived was 48 (80%), and ventricular arrhythmias was documented in seven (11.8%) cases. BNP proved to be a useful marker in predicting ventricular tachycardia by plotting the receiver operating characteristic curve that revealed area under the curve of 69.6%.

Conclusion

BNP levels are a strong, independent predictor of sudden death in patients with ischemic cardiomyopathy after an acute MI.

Keywords:

BNP, STEMI, SCD, LVarrhythmia

Introduction

Natriuretic peptides are those released from the brain, heart, and endothelium, in situation in a response to pressure or volume overload of the ventricles. During the past few years, β-natriuretic peptide (BNP) has been suggested as a promising marker for the prognostication of acute and chronic left ventricular (LV) dysfunction and correlates with the degree of systolic LV dysfunction [1,2]. These peptides are powerful markers for prognosis, diagnosis, and risk stratification in patients with heart failure in all previous studies [3–7]. Few studies [8–11] have investigated if plasma BNP levels are associated with an increased risk of ventricular arrhythmia in patients with acute myocardial infarction. Despite all advances in prevention and treatment of ventricular arrythmia by pharmacological treatment and effectiveness of implantable cardioverter defibrillators (ICDs) as effective therapeutic measure for such problem, ventricular arrhythmia still remains a major cause of sudden cardiac death in these group of patients [12–14].So, risk stratification improvement is need to identify patients at increased risk for ventricular tachycardia (VT), and those patients who would not get benefit, who would only be exposed to potential adverse effects, and who would not get any benefits if at low risk [3,12–14]. To identify the patients who would achieve the maximum benefit from ICD therapy, a relationship between natriuretic peptides and ventricular arrhythmia has been suggested [6,15–18]. So our study aimed to evaluate the importance of BNP levels in predicting the occurrence of malignant arrhythmias in patients with FV dysfunction. After an acute myocardial infarction, BNP is released early on because of ischemia and necrosis of myocardial cells.

Thereafter, BNP increases as a result of systolic or diastolic dysfunction and increased wall stress of the LV [3,4,14].

Patients and methods

This is a prospective observational study conducted on 60 consecutive patients who were diagnosed of developing LV systolic dysfunction after an acute ST-elevation myocardial infarction (STEMI) and admitted to the critical care unit in Kasr El-Aini Hospital, Cairo University, Cairo, Egypt. Our studied population included 60 consecutive patients who were diagnosed to develop LV systolic dysfunction after an acute STEMI.

Inclusion criteria

Adult patients with an acute myocardial infarction (STEMI), only if they were found to have at least two of the following criteria:

(1) Typical retrosternal burning or compressing chest pain (relieved by nitrates).

(2) ST-segment elevation of more than 0.1mV in limb leads or more than 0.2mV in precordial leads or new or indeterminate left bundle branch block.

(3) Cardiac biomarker increase, suggestive of myocardial injury in early few hours.

Moreover, they should have echocardiographic evidence of LV systolic dysfunction [LV ejection fraction (EF) <50%].

Exclusion criteria

The following were the exclusion criteria:

(1) Renal injury defined as serum creatinine level more than 1.5 mg/dl that causes a nonspecific rise of troponin.

(2) Systemic septicemia.

(3) Cardiac arrest before sampling.

(4) Patients with previous or present cerebrovascular stroke.
(5) Advanced or disseminated malignancy.

All cases were subjected to the following:
(1) Informed written consent from the patient or the closest family member.
(2) Full medical history taken from the patient himself or a family member.
(3) Detailed Clinical and cardiac assessment
(4) Surface 12-lead ECG as routine.
(5) Cardiac imaging by transthoracic echocardiographic examination.
(6) Biochemical assessment.

Clinical assessment in the following form:
(1) Full clinical and cardiac examination.
(2) Scoring systems used to predict outcome in heart failure to evaluate patients with heart failure after an acute myocardial infarction (MI):

(1) New York Heart Association clinical functional classification based on degree of severity of symptoms and physical activity assessment.

(a) Class I: No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
(b) Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
(c) Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
(d) Class IV: Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increase.

Surface 12-lead ECG
Twelve-lead ECG with consistent chest leads positioning was performed daily for 5 days. ECG result was considered abnormal if the following was detected:

(1) ST-segment elevation greater than 0.1mV in more than one limb leads or 0.2mV in two or more precordial leads.

(2) Malignant arrhythmias.

Transthoracic echocardiographic examination
Each patient in our studied population was examined in the left lateral position according to the recommendations of the American Society of Echocardiography. Images were obtained from each part of the examination together with standard surface ECG stored for subsequent analysis. The study was conducted using an ATL HDI 5000 colored echocardiographic

machine, using a 3.5-MHz transducer. Two-dimensional and M-mode methods were used for assessment of LVEF.

Biochemical measurement

(1) Full laboratory assessment.

(2) Cardiac biomarkers measurement (cardiac troponin I, creatine kinase, MB, and creatine, measured on admission).

(3) Serum samples were taken from every patient in our study in the first 48 h to measure the level of BNP.

Results

This is a prospective observational study conducted on 60 (adult) patients admitted to critical care unit, Cairo University, with an acute MI who developed post-MI LV systolic dysfunction within the period from September 2014 to March 2015.

Demographic and descriptive data

Our study included 60 adult patients with LV dysfunction, after an acute MI. Mean age in our studied patients was 58.6±8.3 years (range: 35–80 years). Males represented 73.4% of our cases (44 males and 16 females).

Clinical examination

Risk stratification category in our cases revealed mean NYHA of 2.9, Killip class of 2.7, and TIMI risk score of 8.2. as shown in Table 1.

Table 1 Clinical examinations

Clinical examinations	
NYHA	2.9±0.8
KILLIP class	2.7±0.8
TIMI risk point	8.2±2.4

Follow-up clinical examination

Follow-up full clinical and cardiac examination was done for survivors and revealed a mean NYHA of 1.9±0.7. Follow-up was performed for our survived patients within 90 days. We found that only 48 (80%) patients survived from those, and in seven patients, life-threatening arrhythmias were documented on surface ECG (11.8%).

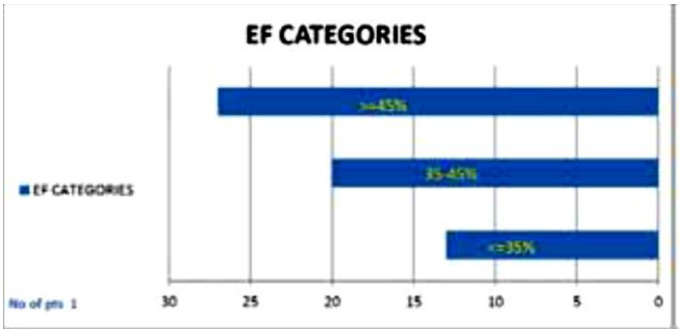
Initial trans echocardiographic examination

All our patients underwent echocardiography and revealed a mean EF of 41.9±7% with regional wall motion abnormalities of 13.3±3.2, as shown in the **Table 2.**

Table 2 Initial echocardiographic examination

Initial echocardiographic examination	
LVEF (%)	41.9±7
RWMA	13.3±3.2

LVEF, left ventricular ejection fraction; RWMA, regional wall motion abnormalities



(Figure1*) Initial ejection fraction (EF) categories.*

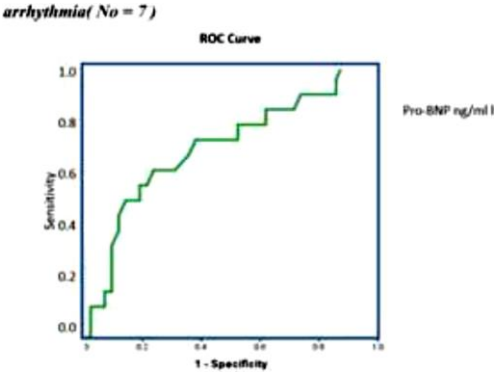
We found that 27 patients had an initial EF value equal or higher than 45%, whereas 20 patients had an EF mean values ranging between 35 and 45%, and only 13 patients had values lower than 35% (Figs 1 and 2).

Follow-up trans echocardiographic examination

Follow-up trans-echocardiographic data were obtained for survived patients and revealed a mean EF value of 46.7±8.9% with regional wall motion abnormalities of 8.7±4.2, as shown in Tables 3 and 4.

Discussion

Despite recent diagnostic and therapeutic improvements, AMI is a major cause of mortality and morbidity. Recently, BNP has been recognized in many studies as a sensitive marker for prognostication of acute and chronic LV failure. In patients who develop an acute STEMI and have higher levels of BNP, the outcome would be worse [7–11]. ICD proved to be the treatment of choice for patients with high risk for occurrence of potentially fatal ventricular arrhythmias [1–3], and it has been increasingly recognized that ICDs are superior to antiarrhythmic drugs in survivors of cardiac arrest or unstable VT [18–20].



(Figure2): *Receiver operating characteristic (ROC) analysis for ventricular tachycardia. BNP, β-type natriuretic peptide.*

Table 3 Echocardiogram examination

	Echocardiogram examination
EF (%)	46.7±8.9
RWMW	8.7±4.2

EF, ejection fraction; RWMA, regional wall motion abnormalities

Table 4 Cutoff value of β-type natriuretic peptide for prediction of occurrence of ventricular arrhythmia (N=7)

Ventricular tachycardia/ VF	AUC	*P* value	Cutoff	Sensitivity (%)	Specificity (%)
BNP (ng/ml)	69.98%	**0.016**	3.14	72.32	61.8

AUC, area under the curve; BNP, β-type natriuretic peptide; VF, ventricular fibrillation.

In certain high-risk groups, ICDs also proved to be more beneficial than drug therapy for primary prevention of SCD [21–24]. For patients with severe ischemic cardiomyopathy, such as the population in our study, this is particularly true, and thus, a better risk identification of patients with depressed ventricular function who could benefit from an ICD or, definitely, more importantly, those who are unlikely to get any benefit would be beneficial regarding cost and also management.

Our study aimed to evaluate the role BNP for better prognostication of high-risk patients for occurrence of ventricular arrhythmia to improve risk stratification in this group of patients.

In addition to all previous reports about sensitivity of such prognostic marker in patients who developed acute heart failure, we also found BNP as a promising marker in predicting malignant arrhythmia in patients with STEMI who developed LV systolic dysfunction, post-MI (ROC curve: 77.5%, P=0.001, sensitivity=70%, specificity=67.5%).Similar to our findings, Yang et al. [24] studied 246 patients with AMI with 14 months of follow-up and investigated several indexes, such as BNP, to determine the most valuable prognostic factors for AMI-induced mortality. They found, with multiple regression analysis, that BNP is an independent risk factor and an appropriate prognostic index for mortality rate estimation, in short term and long term after AMI [25]. However, there are few evidence about BNP levels and major electrical complications. Blangy et al. [26] stated that, together with serving as a marker of left ventricular dysfunction, BNP level is a marker of VT as well, and increased serum BNP was associated with a higher incidence of VT, which is almost the same as we found in our study. Our study revealed the promising role of BNP in predicting VT in patients with ischemic cardiomyopathy after acute STEMI (ROC curve:69.9%, P=0.017, sensitivity=72.2%, specificity=61.9%. Finally, and as we concluded, Emmanuel and colleagues stated that to achieve the maximum benefit from ICD therapy, more precise risk stratification is required, even in high-risk patients with post-myocardial infarction. There is no single powerful predictor of arrhythmic death and effectiveness of prophylactic ICD use.

Conclusion

BNP levels are a promising marker of occurrence of ventricular arrhythmia in patients with ischemic cardiomyopathy after an acute MI.

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Nil.

Conflicts of interest

None.

References

1. Manios EG, Kallergis EM, Kanoupakis EM, Mavrakis HE, Kambouraki DC, Arfanakis DA, Vardas PE. Amino-terminal pro-brain natriuretic peptide predicts ventricular arrhythmogenesis in patients with ischemic cardiomyopathy and implantable cardioverter-defibrillators. Chest 2005; 128:2604–2610.
2. Garrone P, Biondi-Zoccai G, Salvetti I. Quantitative coronary angiography in the current era: principles and applications. J Interv Cardiol 2009; 22:527–536.
3. Josephson M, Wellens HJ. Implantable defibrillators andsudden cardiac death. Circulation 2004; 109:2685–2691.
4. Huikuri HV, Makikallio TH, Raatikainen MJ, Perkiömäki J, Castellanos A,Myerburg RJ, et al. Prediction of sudden cardiac death: appraisal of the studies and methods assessing the risk of sudden arrhythmic death. Circulation 2003; 108:110–115.
5. Maisel AS. B-type natriuretic peptide (BNP) levels: diagnose-tic and therapeutic potential. Rev Cardiovasc Med 2001; 2 (Suppl 2):S13–S18.
6. Berger R, Huelsman M, Strecker K, Bojic A, Moser P, Stanek B, Pacher R,et al. B-type natriureticpeptide predicts sudden death in patients with chronic heartfailure. Circulation 2002; 105:2392–2397.
7. Gardnera RS, Oz ?alpF, Murdaya AJ, Robb SD, McDonagh TA. N-terminal pro-brain natriuretic peptide: a new gold standard in predicting mortality in patients with advanced heart failure. Eur Heart J 2003; 24:1735–1743.
8. Koglin J, Pehlivanli S, Schwaiblamir M, Vogeser M, Cremer P, vonScheidt W. Role of brain natriuretic peptide in risk stratification of patients with congestive heart failure. J Am Coll Cardiol 2001; 38:1934–1941.
9. Harrison A, Morrison LK, Krishnaswamy P, Kazanegra R, Clopton P, Dao Q, et al. B-typenatriuretic peptide (BNP) predicts future cardiac events inpatients presenting to the emergency department with dysnea. Ann Emerg Med 2002; 39:131–138.
10. Tapanainen JM, Lindgren KS, Mäkikallio TH, Vuolteenaho O, Leppäluoto J,Huikuri HV. Natri-uretic peptides as predictors of non-sudden and suddencardiac death after acute myocardial infarction in the-block-ing era. J Am Coll Cardiol 2004; 43:757–763.
11. Heeschen C, Hamm CW, Mitrovic V, Lantelme NH, White HD; Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Investigators. N-terminalpro B-type natriuretic peptide levels for dynamic risk strati-fication of patients with acute coronary syndromes. Circulation 2004; 110:3206–3212.
12. Bassan R, Potsch A, Maisel A, Tura B, Villacorta H, Nogueira MV, et al. Btype natriuretic peptide: a novel early blood marker of acute myocardial infarction in patients with chest pain and no ST-segment elevation. Eur Heart J 2005; 26:234–240.
13. Potocki M, Mair J, Weber M, Hamm C, Burkard T, Hiemetzberger R, et al.Relation of N-terminal pro-B-type natriuretic peptide to symptoms, severity,and left ventricular remodeling in patients with organic mitral regurgitation.Am J Cardiol 2009; 104:559–564.

14. Ray IB, Reddy VY. Implanted defibrillators and primary prevention of sudden cardiac death: where are we today? IntJ Cardiol 2005; 98:15–20.
15. Hansen DE, Craig CS, Hndeghem LM. Stretch-induced arrhythmias in the isolated canine ventricle: evidence for the importance of mechanoelectrical feedback. Circulation 1990; 81:1094–1105.
16. Franz MR, Cima R, Wang D. Electrophysiological effects of myocardial stretch and mechanical determinants for stretch- activated arrhythmias.Circulation 1992; 86:968–978.
17. ReiterMJ. Effects of mechanoelectrical feedback: influence among patients with congestive heart failure. Cardiovasc Res 1996; 32:44–51.
18. ZhuWX, Johnson SB, Brandt R, Burnett J, PackerDL. Impact of volume loading and load reduction on ventricular refractoriness and conduction properties in canine congestive heart failure. J Am Coll Cardiol 1997; 30:825–833.
19. Mukoyama M, Nakao K, Hosoda K, Suga S, Saito Y, Ogawa Y, et al. Brain natriuretic peptide as a novel cardiac hormone in humans. Evidence for an exquisite dual natriuretic peptide system, atrial natriuretic peptide and brain natriuretic peptide. J Clin Invest 1991; 87:1402–1412.
20. YoshimuraM, Yasue H, Okumura K, Ogawa H, Jougasaki M, Mukoyama M,et al. Different secretion patterns of atrial natriuretic peptide and brain natriuretic peptide in patients with congestive heart failure. Circulation 1993; 87:464–469.
21. Maeda K, Tsutamoto T, Wada A, Hisanaga T, Kinoshita M. Plasma brain natriuretic peptide as a biochemical marker of high left ventricular enddiastolic pressure in patients with symptomatic left ventricular dysfunction.Am Heart J 1998; 135:825–832.
22. Maisel AS, Krishnaswamy P, NowakRM, McCord J,Hollander JE, Duc P, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med 2002; 347:161–167.
23. Morrison LK, Harrison A, Krishnaswamy P, Kazanegra R, Clopton P, Maisel A. Utility of a rapid B- natriuretic peptide assay in differentiating congestive heart failure from lung disease in patients presenting with dyspnea. J Am Coll Cardiol 2002; 39:202–209.
24. Yang YJ, Mao Y, Ni XH, Chen JL, Gao RL, Chen ZJ. The predictive value of B-type natriuretic peptide for the mortality from acute myocardial infarction. Zhonghua Nei Ke Za Zhi 2007; 46:450–453.
25. 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 acrossthe whole spectrum of acute coronary syndromes. Circulation 2004; 110:128–134.
26. Blangy H, Sadoul N, Dousset B, Radauceanu A, Fay R, Aliot E, Zannad F.Serum BNP, hs-C-reactive protein, procollagen to assess the risk of ventricular tachycardia in ICD recipients after myocardial infarction. Europace 2007; 9:724–729.