Brain Natriuretic Peptide as a Predictor of Major Adverse Cardiac Events after Successful Percutaneous Coronary Intervention

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Abstract

B-type natriuretic peptide (BNP) has diagnostic and prognostic value in a wide variety of cardiac disorders including heart failure and coronary artery disease; however, it is value in Percutaneous Coronary Intervention (PCI) is not well established.

The aim of the work is to assess whether serum BNP level just before PCI has a predictor value of Major Adverse Cardiac Events (MACE) during hospitalization (as recurrent chest pain, new or worsening heart failure, significant arrhythmia and in-hospital mortality) and after 3 months follow up (as echocardiography assessing left ventricular dysfunction, rest chest pain, hospitalization for Acute Coronary Syndrome (ACS) or heart failure, revascularization and cardiac mortality).

In 82 consecutive patients with Coronary Artery Disease (CAD), plasma BNP levels were measured immediately before successful PCI. Patients were followed for 3 months for the occurrences of MACE. The patients were divided into 2 groups according to occurrence of composite end points of MACE at follow-up; MACE (-) Group: 45 patients who did not have MACE and MACE (+) Group: 37 patients who had MACE.

A statistically significant positive correlation between higher BNP levels and occurrence of MACE (P-value < 0.001)

Keywords

B-type natriuretic peptide, Coronary artery disease and Percutaneous Coronary Intervention.

Introduction

The diagnostic value of BNP and NT-proBNP was primarily been investigated in patients with

heart failure. In a large number of studies, it has consistently been found that BNP and NT-proBNP levels are elevated in patients with heart failure; moreover, the levels of BNP and NT-proBNP have been found to be related to disease severity, as indicated by functional class (New York Heart Association class), left ventricular systolic ejection fraction and left ventricular diastolic function [1].

Independent of their diagnostic value, several large-scale studies have convincingly demonstrated that high BNP and NT-proBNP levels provide strong prognostic information for an unfavorable outcome (e.g. death, cardiovascular death, and readmission to hospital or cardiac events) in patients with heart failure or asymptomatic left ventricular dysfunction [2].

In multivariable models, BNP and NT-proBNP has shown to be superior to other prognostic parameters and, in some studies, even to be the only independent prognostic factors. Head-to-head studies comparing the diagnostic performance of BNP and NT-proBNP testing were been performed in patients with heart failure and patients with asymptomatic left ventricular dysfunction. These studies showed that both markers performed equally well, with almost identical areas under the receiver operating characteristics curves [3].

Thus, it was concluded from these studies that there is no meaningful difference between the markers in terms of risk stratification in clinical routine.

Originally, BNP and NT-proBNP were considered to be biomarkers of heart failure. More recently, however, there is a growing body of data on the relevance of both markers in CAD. It is widely believed that the underlying pathophysiological process for an increase in BNP and NT-proBNP levels is left ventricular systolic or diastolic dysfunction due to myocardial ischemia leading to increased wall stress. Nevertheless, data derived from experimental studies suggest that there is a direct

release of BNP and NT-proBNP from cardiomyocytes in response to myocardial ischemia, independent of ventricular wall stress [4, 5].

In agreement with these experimental findings, it has been shown that BNP levels increase even after temporary myocardial ischemia induced by balloon inflation during coronary interventions [6].

The initial studies of BNP in acute coronary syndromes (ACS) were small case-control studies, limited mostly to patients with ST-elevation MI, who are likely to have at least minor LV dysfunction. More recently, the prognostic application of BNP has been extended to include patients with unstable angina and non-ST-elevation myocardial infarction (NSTEMI) [7]. Several studies have come up showing that basal BNP levels in acute MI patients predict short and long term prognosis [8-13].

Patients and methods

Aim of work is to assess if serum BNP level just before PCI has a predictor value of Major Adverse Cardiac Events (MACE); after successful coronary intervention during hospitalization (as recurrent chest pain, new or worsening heart failure, significant arrhythmia and in-hospital mortality) and after 3 months follow up (as changes in assessment of left ventricular (LV) functions by trans-thoracic echocardiography, rest chest pain, hospitalization for ACS or heart failure, revascularization and cardiac mortality).

This study enrolled 82 consecutive patients admitted to coronary care unit at Cardiovascular Department – Fayoum University Hospital and 6 October Insurance Hospital – Al Doky – Giza, who underwent successful elective or primary percutaneous coronary intervention for Stable CAD (SCAD) or ACS (Unstable Angina,

NSTEMI and STEMI) in the period from June 2018 to December 2018.

All patients were subjected to detailed history taking, clinical examination, 12-lead ECG, laboratory measurement of BNP within one hour before PCI and serum creatinine level, trans-

thoracic echocardiography assessment of left ventricular systolic function before PCI and after three months using modified Simpson's technique [14] and observation for the occurrence of MACE before discharge and within three months after discharge.
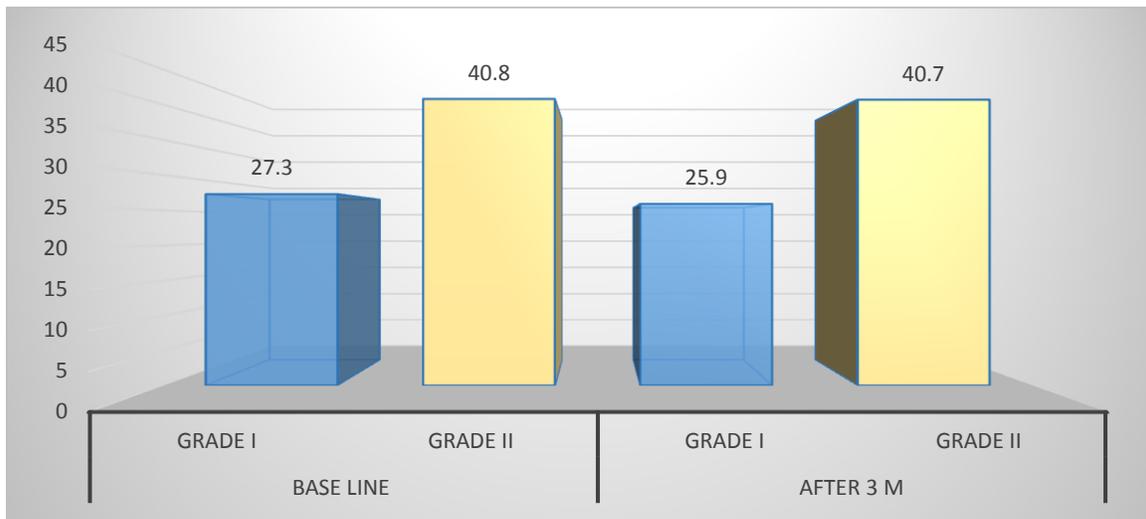
Results

1. This study revealed that there was statistical significance prediction of MACE to BNP level [P-value < 0.001] and diastolic dysfunction during the 3 months follow up [P-value < 0.008].

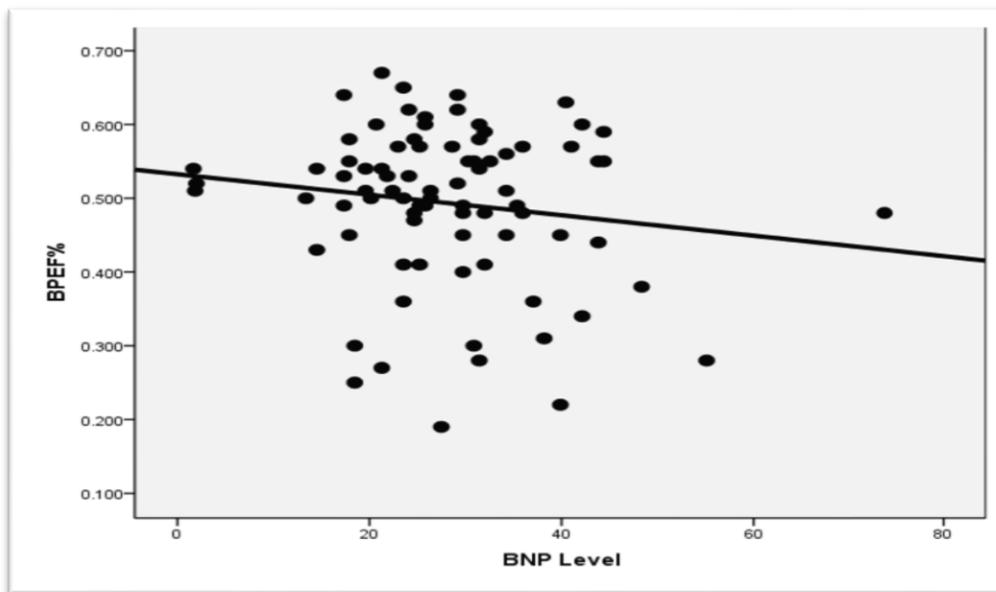| Variables	B	S.E	Wald	Sig.	OR	CI
DD	-2.4	1.7	1.9	0.2	0.09	0.003-2.63
DD (3m)	3.8	1.4	7.1	**0.008**	44	2.7-708.2
BNP	4.6	0.9	26.2	**<0.001**	103	14.5-605.4

2. There is statistically significant difference in BNP level between degree of diastolic dysfunction with high mean BNP level among grade II diastolic dysfunction at presentation and after 3 months follow up [P-value < 0.05].

Variables		BNP level		p-value	Sig.
		Mean (pg/ml)	SD		
Base line DD	Grade I	27.3	10.1	**0.003**	**HS**
	Grade II	**40.8**	16.8		
DD after 3 months	Grade I	25.9	9.2	**0.001**	**HS**
	Grade II	**40.7**	12.7		

3. There is no statistically significant correlation between BNP level and EF at base line presentation [P-value > 0.2]. On the other hand there is statistically significant negative correlation between BNP level and EF after 3 months; which indicated that increase in BNP level will be associated with decrease in EF [P-value < 0.01].

EF%	BNP level		
	r	p-value	Sig.
Base line	-0.15	0.2	NS
After 3 months	**-0.28**	**0.01***	**S**

Discussion

> In our study, there was a statistically significant positive correlation between higher BNP levels and occurrence of MACE (P-value < 0.001). 39 patients had higher BNP level for their age; 87.2 % of them had MACE and 91.9 % of the MACE positive group had high BNP level for their age. Plasma BNP levels in MACE Positive group were significantly higher than that of MACE Negative group [37.02 pg/ml ± 6.5 SD vs. 21.04 pg/ml ± 10.2 SD and P-value <0.001].

Multiple logistic regression analysis identified that BNP as an independent predictor of MACE during the three months follow up period [OR 103, CI 14.5 – 605.4, P-value <0.001]; considering a BNP level of 37 pg/ml ± 6.5 is a threshold for patients who are at higher risk for incidence of MACE.

These findings were consistent with the following studies:

Assessment of BNP before PCI and its association with major adverse cardiac events in acute coronary syndrome with heart failure [15]: This study enrolled 150 patients who were followed up for 30 days and concluded that pre PCI BNP and elderly age are strong predictors of major adverse cardiac events at 30 days in patients presenting with acute coronary syndrome with clinically evident heart failure.

Evaluation of B-Type Natriuretic Peptide for Risk Assessment in Unstable Angina/Non–ST-Elevation Myocardial Infarction [16]: This study enrolled 1676 patients who were followed up for six months and concluded that elevated BNP (>80 pg/ml) at presentation identifies patients with non–ST-elevation ACS who are at higher risk of death and CHF and adds incremental information to cTnI.

Value of peri-procedural B-type natriuretic peptide levels in predicting cardiac events after elective percutaneous coronary intervention [17]; a study done in 2008 that enrolled 95 patients with SCAD who underwent elective PCI and followed up for 12 months. Blood samples for BNP were obtained before, 1 hour and 24 hours after PCI. The study showed that all measured plasma BNP levels were significantly higher in patients with MACE compared to those free of MACE.

> In our study there was no statistically significant correlation between BNP level and Ejection Fraction (EF) at base line presentation [P-value > 0.2]. On the other hand there is statistically significant negative correlation between BNP level and EF after 3 months; which indicated that increase in BNP level will be associated with decrease in EF [P-value < 0.01], and there was statistically significant difference in BNP level between degree of diastolic dysfunction with high mean BNP level among grade II diastolic dysfunction at presentation and after 3 months follow up [P-value < 0.05].

These findings were consistent with the work done in 2016 in a study [18]; named, Correlation between brain natriuretic peptide levels and the prognosis of patients with left ventricular diastolic dysfunction; that enrolled 708 patients who were followed up for 20-51 months. Endpoints were defined as mortality or

readmission due to cardiovascular disease, or mortality due to any other reason. The study showed that the prognoses of patients with elevated BNP levels were correspondingly worse when compared with patients with lower BNP levels. This correlation was demonstrated to be significant in patients with LV diastolic dysfunction.

Study Limitations

1. The small sample size of patients that was enrolled in the study.
2. Our study was not a randomized and controlled study. As a result, we could not exclude the influence of many other unmeasured variables.
3. The dosage of and adherence to medications could not be assessed through our registry. Variations in the use of the appropriate medications could have led to substantial differences in MACE among our patients.

Conclusion

1. High levels of plasma BNP collected just before successful Percutaneous Coronary Intervention in patients with Coronary Artery Disease are associated significantly with Major Adverse Cardiac Events (MACE) during hospitalization and 3 months follow up.
2. The plasma BNP collected just before successful Percutaneous Coronary Intervention in patients with Coronary Artery Disease is an independent predictor of MACE during the three months follow up period.

Acknowledgement

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