

Serum N-Terminal pro Brain Natriuretic Peptide as Predictor of Left Ventricular Remodeling in hypertensive Subjects with Acute Coronary Syndrome

Wafa M. Merza, PhD⁽¹⁾

¹Department of basic science, Collage of dentistry, University of Baghdad

Abstract

Background:

Acute Coronary Syndrome (ACS) refers to any group of acute symptoms and sign, attributed to sever obstruction of the coronary arteries . N-terminal pro-BNP (NT-proBNP), are secreted by human atrial and ventricular myocardium. The rise in BNP and NT-pro BNP levels after STEMI correlates with infarct size and regional wall motion abnormalities. Echocardiography remains the most frequently used and usually the initial imaging test to evaluate all cardiovascular diseases related to a structural, functional, or hemodynamic abnormality of the heart or great vessels. High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing.

The aim of the study:

1-To determine the usefulness of NT-PRO Brain Natriuretic Peptide ,hs-troponin I and hs C-reactive protein as a biochemical indicator in early diagnosis of ischemia.

4- To correlate the studied biochemical markers and Echocardiographic parameters with the risk factor of cardiac ischemia (High blood pressure).

Subjects and Methods:

Seventy patients with acute coronary syndrome and twenty healthy individuals as control group are included in the present study. Clinical, echocardiographic, and laboratory characteristics, including N –Terminal pro brain natriuretic peptide (NT-PRO BNP), troponin I (TnI), and C-reactive protein (CRP) were measured within 24 hours of hospitalization for 70 patients, they divided into two groups according to Blood pressure level (hypertensive patients were hypertensive {On antihypertensive drug(s) or blood pressure above 140/90 mmHg} & non hypertensive). The present study was conducted at the Department of Bio Chemistry, College of Medicine, University of Baghdad and Baghdad Teaching Hospital during the period from April 2020 to April 2021.

Results:

The results showed that, acute coronary syndrome are more common among male patients. The patients with acute coronary syndrome are found to have significantly higher mean (\pm SEM) value of serum NT-PROBNP and CRP when compared with that of control group ($p \leq 0.05$), the mean (\pm SEM) value of serum troponin I was non significantly higher as compared with the mean (\pm SEM) value of serum control group ($p > 0.05$).

The mean(\pm SEM) values of NT-PROBNP, left atrium diameter and E/e were non significantly lower in hypertensive group than non hypertensive group, while mean(\pm SEM) values of hs-troponin I, hs-CRP, isovolumic relaxation time and ejection fraction were found non significantly higher in non hypertensive group than hypertensive group.

Conclusions

NT-PRO BNP was a useful biochemical marker in the diagnosis` of ischemia. NT-PRO BNP was more sensitive than troponine I for diagnosis of ischemia, it level lower in hypertensive group than non-hypertensive group. There were no significance difference in echocardiographic parameters in the presence or absence of HT.

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I. Introduction

Acute coronary syndrome (ACS) refers to any group of symptoms attributed to sever obstruction of the coronary arteries. The most common symptom prompting diagnosis of ACS is chest pain, often radiating to the left arm or angle of the jaw, pressure-like in character, and associated with nausea and sweating.¹

Risk Factors

Atherothrombosis can no longer be considered a disease of the developed world, because myocardial infarction and stroke are increasingly prevalent worldwide, across all socioeconomic strata. By 2025,

cardiovascular mortality on a worldwide scale will likely surpass that of every major disease group, including infection, cancer, and trauma.²

High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing. Part of the complexity of hypertension as a risk factor relates to changing definitions of risk and an understanding that systolic blood pressure and pulse pressure may have greater importance than diastolic blood pressure, contrary to decades of clinical teaching. Most epidemiologic studies now recognize the joint contributions of systolic and diastolic blood pressure to the development of cardiovascular risk, an issue that has influenced strategies for risk detection. Isolated systolic hypertension, in particular, has at least as much importance as diastolic blood pressure for the outcomes of total cardiovascular mortality and stroke. Evidence supports the treatment of systolic hypertension, even in older adult.³

Isolated systolic hypertension thus appears to represent a distinct pathophysiologic state in which elevated blood pressure reflects reduced arterial elasticity not necessarily associated with increased peripheral resistance or an elevation in mean arterial pressure. Pulse pressure, generally reflecting vascular wall stiffness, also predicts first and recurrent myocardial infarction. Defined as the difference between systolic and diastolic blood pressures, pulse pressure appears to predict cardiovascular events independently, particularly heart failure.⁴

II. Aim of the study

1-This study was designed to investigate and assess the serum concentrations of some biochemical markers in patients with Acute Coronary Syndrome and to define the role of these biochemical markers in the diagnosis of such patients. The investigated biochemical markers include; NT-proBNP, in addition to cardiac hs-TnI and hs-CRP.

2-To correlate NT-PRO Brain Natriuretic Peptide levels and echoparameters (diameter of left atrium, E/e, deceleration time, ejection fraction, isovolumic relaxation time, mitral regurgitation and diastolic function) with the risk factors of ACS like hypertension

III. Patients and Methods

Study Design and Population.

Patients with ACS admitted consecutively between April 2020 and April 2021 to a cardiology emergency single center in Baghdad Teaching Hospital were prospectively evaluated with their data registered in the institution's database. Baseline clinical and admission laboratory characteristics, CAD risk factors, medicines used, in-hospital outcomes, ECG, and treatments were observed. The Ethics Committee of the hospital approved this study. A total of 70 ACS patients were included and divided into two groups according to Blood Pressure (hypertensive & non hypertensive patients were hypertensive {On antihypertensive drug(s) or blood pressure above 140/90 mmHg}), and 20 healthy subjects as control.

Data Collection.

From each patient (within 24 h from admission) and control, three ml of venous blood were aspirated from a suitable vein. Samples were collected between (8-9 A.M.). Blood samples were transferred for storage to measure the serum levels of (NT-PROBNP, hs-CRP, and hs-Troponin I). The non heparinized blood in the plain tubes were left to clot and then centrifuged by cold centrifuge at 4000 rpm for 5 minutes many times (1-5) to separate the serum and dispensed into tightly closed Eppendorf tubes 1.0 ml and stored at -20 C° until assayed.

Each serum sample was analyzed for urea and creatinin to exclude kidney diseases. **Biochemical parameters included in this study:**

1- N-terminal pro-brain natriuretic peptide(NT-PROBNP) level was measured by using ELIZA Kits from Biosource, Incorporation.USA. Cat.No : MBS294727.

2-Hs C-Reactive Protein (CRP) level was measured by using ELIZA Kits from Demeditec Diagnostics GmbH, Lise-Meitner-Str.2, 24145 Kiel, Germany, and hs- cardiac troponin I (hs-cTnI) level was measured by using ELIZA Kits from Biosource, Incorporation.USA. Cat.No : MBS165910.

Echocardiographic parameters were measured in all patients by consultant cardiologists at echocardiographic unit/ Baghdad Teaching Hospital, they involved:

1-Diameter of left atrium

2- E (left ventricular inflow velocity) / e (tissue doppler velocity) ratio to estimate ventricular filling pressure.

3-Isovolumic relaxation time

4-Deceleration time

5-Left ventricular Ejection Fraction

Statistical Analysis:

The Statistical Analysis System- SAS (2019) was used to show effect of different factors in study parameters. Data analysis was done using chi- square test for tables with frequencies, while independent sample t-test was used for tables with means, standard deviation and standard error mean. P value of < 0.05 was used as the level of significance.

IV. Results

Clinical data

This study included 70 patients with mean±SD of age was (58.77±11.45) years ranged from (25-84) years divided into two groups: Male group included 52(74.3%) patients, and female group included 18 (25.7%) patients.

The control group included 20 healthy persons with mean age (33.47±12.58) years and ranged from (20-58) years, divided into two groups male group included 10 (50%) persons and female group included 10 (50%) persons, table(1),(2).

patients mean age was significantly higher than control group mean age(P-value =0.0149). There was a significant increase in the frequency of ACS among males in comparison to females(P-value =0.0027).

Table(1)Frequency distribution of total study sample by age.

	Control	patients	P-value
Mean± SD	33.47±12.58	58.77±11.45	0.0149 **
SE	1.49	1.36	--
Min	20	25	--
Max	58	84	--
C.V%	37.6089	19.48	--

Table (2) Frequency distribution of total study sample by gender.

Sex	Control		patients	
	No.	%	No.	%
Male	10	50	52	74.3
Female	10	50	18	25.7
Total	20	100	70	100
P-value	---	1.00 NS	---	0.0027 **

The mean (± SEM) value of Female patients age was significantly higher as compared with mean (± SEM) value of Male patients age,(p –value= 0.021) .

There was a non-significant increase in the frequency of males with History of IHD and Obesity in comparison to females.

Biochemical markers in Acute Coronary Syndrome (ACS) patients and control group

Serum level of NT-PRO Brain Natriuretic Peptide (NT-PROBNP), (hs-TnI) and (hs-CRP) were compared between the patients group and the control group using analysis of variance (ANOVA) and t-test of significant as in table (3). The patients with ACS were found to have significantly higher mean (± SEM) value of serum NT-PROBNP concentrations (p=0.0144) as compared with mean (± SEM) value of serum control group, the mean (± SEM) value of serum hs-troponin I concentrations did not differ significantly (p=0.372) as compared with mean (± SEM) value of serum control group, and significantly higher mean (± SEM) value of serum hs-CRP concentrations (p=0.002) as compared with mean (± SEM) value of serum control group.

Table (3) Comparison between patients & control according to biochemical markers.

Group	No.	Mean ± SEM Mean ± SD		
		NT-PROBNP (ng/L)	TnI: Troponin I (ng/L)	CRP:C-Reactive protein (mg/L)
Patients	70	203.95 ± 21.42	8.10 ± 0.87	12.73 ± 0.97
		203.95 ±179.21	8.10 ±7.27	12.73 ±8.11
Control	20	107.79 ± 4.23	7.74 ± 0.48	0.316 ± 0.143
		107.79 ±18.91	7.74 ±2.14	0.316 ±0.63
T-test value	--	34.782 **	1.973 NS	3.019 ***

P-value		0.0144	0.372	0.00252
** (P≤0.01), *** (P≤0.001), NS: Non-significant (p >0.05).				

- Results expressed as Mean (+ SEM).
- Results expressed as Mean (± SD).

Hypertension

Forty-four patients out of seventy with ACS patients were hypertensive {On antihypertensive drug(s) or blood pressure above 140/90 mmHg}, mean(± SEM) values of NT-PROBNP, left atrium diameter and E/e were non significantly lower in hypertensive group than non hypertensive group, while mean(± SEM) values of hs-troponin I, hs-CRP, isovolumic relaxation time and ejection fraction were found non significantly higher in non hypertensive group than hypertensive group, (table 4).

Table (4) Effect of Hypertension on biochemical markers & echocardiographic parameters (Mean ± SEM).

Parameters	Non Hypertensive (No. = 26)	Hypertensive (No. = 44)	P-value
NT-PROBNP(ng/L)	217.00 ± 23.18	196.25 ± 27.04	0.755 NS
hsTnl: TroponinI(ng/L)	8.49 ± 0.76	7.87 ± 0.62	0.386 NS
hs-CRP:C-reactive protein(mg/L)	14.08 ± 1.25	11.94 ± 1.09	0.366 NS
LAD: Left atrium diameter (cm)	3.57 ± 0.82	3.64 ± 0.71	0.504 NS
E/e	9.17 ± 0.76	9.71 ± 0.53	0.591 NS
IVRT:Isovolumic relaxation time (ms)	89.38 ± 7.60	87.74 ± 9.03	0.588 NS
DT:Deceleration time(ms)	184.62 ± 18.37	199.45 ± 16.42	0.407 NS
EF%:Ejection fraction	51.31 ± 4.28	49.09 ± 4.02	0.759 NS
NS: Non-significant.			

V. Discussion

4.1 Clinical data

Age is a strong risk factor for atherosclerotic diseases in western countries. In the present study, the majority of patients who developed UA and AMI were above the age of 40 years and there was a significant increase in the frequency of IHD with increasing age, table (1), the mean age (years) for patients was (58.77±11.45). This result was the same as that of Ibrahim (2007)⁵ who found that mean age for patients with IHD in Erbil was 58 years and this indicated that most of the patients were in their middle age. This result also agree with a study of Mackness et al. (2008) who stated that as you get older, your risk for atherosclerosis increases.⁶ Atherogenesis was considered with distinct chronologic phases. The first phase, initiation occurs all too frequently during childhood or adolescence, then the nascent lesion which enters a phase of progression, that generally considered to occur during young adulthood through middle life. Ultimately, atherosclerotic disease becomes manifested with either chronic, stable symptoms or thrombotic complications such as acute myocardial infarction or ischemic stroke. Traditionally, the latter phase of atherothrombosis, complication occurs in the middle-age or in elderly individuals.⁷

Its also found that the frequency of male patients group were (74.3%) patients, and female group were (25.7%) patients, table(2). So there was a significant increase in the frequency of MI and UA among males in comparison to females, these results agree with the study reported by Villar et al. (2008) who found greater incidence of CVD in men and postmenopausal women compared with premenopausal women implies a vasoprotective phenotype of females, which may be influenced by sex hormones. These hormones, particularly estrogen, have modulator effects on the endothelium and circulating cells that have been implicated in vascular inflammation and in the development of CVD.⁸

Measuring serum NT-PROBNP for patients with ACS showed that the mean (± SEM) value was significantly higher when compared with mean (± SEM) value of serum control group, table(3). B-type natriuretic peptide (BNP) is a counter-regulatory peptide hormone predominantly synthesized in the ventricular myocardium. BNP is released into the circulation in response to ventricular dilatation and pressure overload, thus it reflects ventricular wall stress and tissue hypoxia rather than cell injury perse.⁹ It is a well known marker of left ventricular dysfunction and heart failure (HF), and it provides prognostic information beyond and above left ventricular ejection fraction (LVEF) in patients with acute coronary syndromes (ACS).¹⁰

Hypertension

The mean(\pm SEM) values of NT-PROBNP, left atrium diameter and E/e were non significantly lower in hypertensive group than non hypertensive group, while mean(\pm SEM) values of hs-troponin I, hs-CRP, isovolumic relaxation time and ejection fraction were found non significantly higher in non-hypertensive group than hypertensive group, (table 4).

Kohno M et al.¹¹ have demonstrated that long term therapy with ACEI can reduce elevated concentrations of ANP and BNP in hypertensive patients, 21 patients in the present study were on ACEI therapy, and that the reduction in BNP is closely related to diminishing LV mass. In contrast, there is no significant relationship between reductions in BNP and mean blood pressure. Thus, changes in plasma BNP appear to reflect the magnitude of regression of LVH rather than changes in blood pressure level during antihypertensive treatment. Animal study¹² and clinical study¹¹ of BNP and LVH suggest that the regression of LVH by ACEI therapy may cause reduced secretion of BNP from cardiac ventricles.

Several explanations have been advanced for the close relation between reductions in plasma BNP concentration and those in LV mass. **First**, LV mass and LV synthesis of BNP may have been reduced concomitantly by long-term blockade of angiotensin II in the heart. In fact, angiotensin II is related to BNP secretion from cardiomyocytes as well as the growth of cardio myocytes.¹³ plasma BNP concentration may be a useful marker for LVH during antihypertensive therapy in essential hypertensive patients. LVH increases the hypertensive patient's risk of cardiovascular events, cardiovascular death, and all cause mortality.¹⁴ The risks are maximized when the patient has concentric hypertrophy, with increases in both relative wall thickness and mass.¹⁵

Plasma BNP may be valuable as a prognostic predictor in hypertension.¹⁶ BNP As a Novel Form of Therapy for Hypertension. There are two published reports of the effects of exogenous BNP infused in patients with hypertension. Richards et al.¹⁷ infused human BNP over a period of 2 h in six male patients with untreated, uncomplicated, mild to moderate essential hypertension. Achieved intra infusion plasma BNP immune reactivity was similar to levels previously observed in heart failure or severely complicated hypertension. Plasma cyclic GMP increased, sodium excretion rose 2.5-fold, and plasma aldosterone fell to 50% of placebo values. Blood pressure and heart rate were unchanged. Their data suggest that in essential hypertension, pathophysiological plasma concentrations of human BNP have significant, acute effects that promote natriuresis and suppress plasma aldosterone.

La Villa et al.¹⁸ found that infused BNP induced progressive reductions in left ventricular end-diastolic volume and end-systolic volume, whereas stroke volume did not show any significant change. Cardiac output, arterial pressure, and peripheral vascular resistance did not change significantly.

L Lorgis et al.¹⁹ suggested that comorbidities such as diabetes and hypertension have little impact on NT-proBNP in older people with myocardial infarction.

VI. Conclusions

NT-PRO BNP was a useful biochemical marker in the diagnosis` of ischemia. NT-PRO BNP was more sensitive than troponine I for diagnosis of ischemia, it level lower in hypertensive group than non-hypertensive group. There was no significance difference in echocardiographic parameters in the presence or absence of HT.

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