

## The Correlation between Serum Level of N-Terminal Pro-B-type Natriuretic Peptide and Gensini Score in Patients with Acute Coronary Syndrome

Mohammad Hassan Namazi <sup>1</sup>, Hossein Vakili <sup>1</sup>, Mahsa Charkhkar <sup>1,\*</sup>, Latif Gachkar <sup>2</sup>, Isa Khaheshi <sup>1</sup>

<sup>1</sup> Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup> Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding author: Mahsa Charkhkar, Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel: +98-2122083106, E-mail: m.drcharkhkar@yahoo.com

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### Abstract

**Introduction:** N-terminal pro-B-type natriuretic peptide (NT-proBNP) has emerged as an important biomarker for developing the diagnosis and prognosis of cardiovascular diseases, as several studies have shown that serum levels of NT-proBNP elevate in acute coronary syndrome (ACS) and coronary artery disease (CAD). We performed this study to find any possible correlation between serum levels of NT-proBNP and Gensini score in patients diagnosed with ACS.

**Methods:** In a cross-sectional study, 100 consecutive patients with ACS who were candidates of angiography were recruited and their serum levels of NT-proBNP, Gensini scores, lipid profiles and troponin I levels were measured.

**Results:** Sixty six male and 34 female patients with a mean age of 57.5 years, including 44 with unstable angina, 33 with ST-elevation myocardial infarction, and 23 with non-ST-elevation myocardial infarction were enrolled. The mean serum NT-proBNP level and the Gensini score were 1987.16 pg/mL (17.9-8841) and 31.09 (6-92.5), respectively. The serum NT-proBNP levels and Gensini scores were significantly correlated with a Spearman correlation coefficient of 0.953 ( $P < 0.001$ ). Serum levels of NT-proBNP were not different in patients with single-vessel disease, 2-vessel disease and 3-vessel disease ( $P = 0.257$ ). NT-Pro-BNP levels were also correlated positively with troponin I levels (correlation coefficient = 0.779) and negatively with left ventricular ejection fraction (correlation coefficient = -0.55). Smoker patients had higher NT-proBNP levels ( $P = 0.047$ ). Neither Gensini scores nor NT-Pro-BNP levels had significant correlation with lipid profile or blood sugar.

**Conclusions:** NT-proBNP is directly correlated with Gensini score in patients with ACS and might be used as an important marker for risk stratification in those patients.

### INTRODUCTION

During recent years, new cardiac biomarkers have been explored as useful tools for diagnosis and risk stratification in patients with cardiovascular diseases including acute coronary syndrome (ACS) and coronary artery disease (CAD). One of the biomarkers that have been studied and shown promise in clinical practice is N-terminal pro-B-type natriuretic peptide (NT-proBNP). BNP is synthesized as a 108-aminoacid-long prohormone termed proBNP and secreted mainly from cardiac atrial and ventricular myocardium in response to increases in wall stress or inflammation

[1-4]. After secretion, this propeptide is divided into its biologically active BNP and the NT-proBNP.

Several studies have shown that serum levels of NT-proBNP elevate in a variety of functional and structural cardiac abnormalities, especially ACS and CAD [4-11]; therefore, NT-proBNP has emerged as an important biomarker for developing diagnosis and prognosis for cardiovascular diseases [12-14]. Some studies have reported the beneficial effects of NT-proBNP as a prognostic marker for predicting CAD severity based on angiographic findings [10, 15-18] as well as infarct size and myocardial function after myocardial infarction (MI) [11, 19, 20]. Meanwhile, other studies have

suggested the predictive role of this peptide for assessing long-term mortality of patients with CAD [21-23]. Providing the establishment of NT-proBNP as an approved biomarker for risk stratification and predicting CAD severity in patients with ACS, measurement of this peptide as a non-invasive rapid and simple method can replace other invasive and costly procedures.

Based on these evidences, we performed this study to evaluate whether serum level of NT-proBNP is an appropriate predictor of CAD severity in patients with ACS. To achieve this goal, we tried to find any possible correlation between serum levels of NT-proBNP and Gensini scores in patients diagnosed with ACS.

## METHODS

In a cross-sectional study, 100 consecutive patients, admitted in CCU of Shahid Modarres Hospital (a university hospital affiliated to Shahid Beheshti University of Medical Sciences in Tehran, Iran) in 2012 with diagnosis of ACS, were recruited. They included patients with unstable angina (UA), ST-elevation MI (STEMI), and non-ST-elevation MI (NSTEMI). Patients with ACS who were candidates of angiography were offered to participate in the study and in case of consent, a questionnaire was filled for each of them comprising their basic medical and demographic information. Twenty four hours after patients' last episode of chest pain, 5 mL of their venous blood was taken and their serum levels of NT-proBNP, troponin-I and creatinine, low-density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol, triglyceride (TG) and blood sugar were measured. Levels of NT-proBNP were measured by Enhanced Chemi luminescence (ECL) using Pro-BNP kit (Roche, Germany).

Patients underwent angiography by expert attending physicians. According to the angiograms, patients were divided into patients with single-vessel disease (SVD), 2-vessel disease (2VD), 3-vessel disease (3VD) and patients with isolated or concomitant left main artery (LM) involvement. The Gensini score was calculated for each patient from the coronary arteriogram by assigning a severity score to each coronary stenosis, according to the degree of luminal narrowing and its geographic importance. Reduction in the lumen diameter, as well as the roentgenographic appearance of concentric lesions and eccentric plaques were evaluated (reductions of 25%, 50%, 75%, 90%, 99%, and complete occlusion were given Gensini scores of 1, 2, 4, 8, 16, and 32, respectively). Each principal vascular segment was assigned a multiplier in accordance with the functional significance of the myocardial area supplied by that segment: the left main coronary artery  $\times 5$ ; the proximal segment of left anterior descending coronary artery (LAD)  $\times 2.5$ ; the proximal segment of the circumflex artery  $\times 2.5$ ; the mid-segment of the LAD  $\times 1.5$ ; the right coronary artery, the distal segment of the LAD, the posterolateral artery and the obtuse marginal artery  $\times 1$ ; and others  $\times 0.5$  [24, 25]. Angiograms were read by two independent readers blinded to patients' data and then averaged.

The exclusion criteria were creatinine  $> 1.5$  mg/dL, fever, body mass index  $> 30$ , left ventricular ejection fraction (EF)  $< 40\%$ , age  $> 75$  years, and sever hepatic or pulmonary diseases. We used SPSS software version 15 for data anal-

ysis. Quantitative variables are presented as mean. T-test and ANOVA were used for comparing two or multiple variables. To find any possible correlation of Gensini scores and serum levels of NT-proBNP with other variables, Pearson's and Spearman's correlation tests were used. A P value of  $< 0.05$  was considered as statistically significant.

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. A written informed consent was obtained from each participant according to the Declaration of Helsinki.

## RESULTS

Among 100 patients enrolled in the study, 66 were male and 34 were female. The mean age of the participants was  $57.5 \pm 19.6$  years; 44 had UA, 33 had STEMI and 23 had NSTEMI. Regarding their EF, 46% had EF of 60% or higher, 17% had EF of 55-60%, 36% had EF of 50-55% and one patient had an EF of 45-50%. Fifty four patients were smokers. Laboratory and clinical results of the patients are shown in Table 1. The mean serum levels of troponin I and NT-proBNP and the mean Gensini score were  $11.3 \mu\text{g/L}$  (range:  $< 0.05$  to 53),  $1987.16 \text{ pg/mL}$  (range: 17.9-8841), and 31.09 (range: 6-92.5), respectively. Angiography showed that 19% of the patients had SVD, 48% had 2VD, 27% had 3VD and the other 6% had isolated or concomitant LM involvement. Of the patients, 79% had isolated or concomitant LAD involvement and LAD was not found in the remaining 21% of the patients.

**Table 1:** Laboratory and Clinical Results of the Patients

Variable	Result
Creatinine (mg/dL)	$1.09 \pm 0.1$
Blood sugar (mg/dL)	$182.7 \pm 83.8$
LDL (mg/dL)	$115.8 \pm 21.8$
Triglyceride (mg/dL)	$321.8 \pm 76.9$
Cholesterol (mg/dL)	$277.2 \pm 58.0$
HDL (mg/dL)	$44.03 \pm 7.7$
Systolic blood pressure (mmHg)	$140.0 \pm 16.2$
Diastolic blood pressure (mmHg)	$84.1 \pm 9.3$

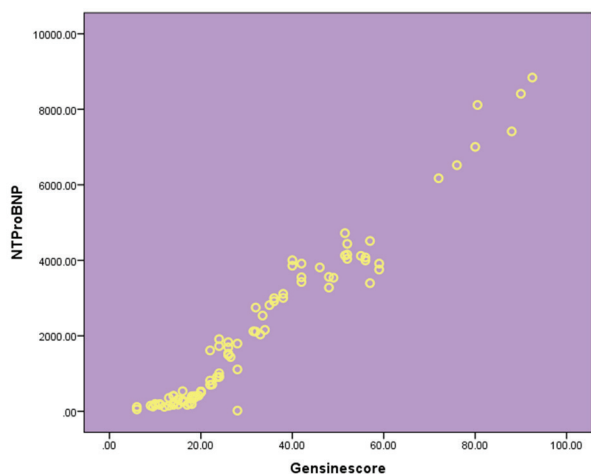
Data in table are presented as Mean  $\pm$  SD.

LDL: Low-density lipoprotein; HDL: High-density lipoprotein

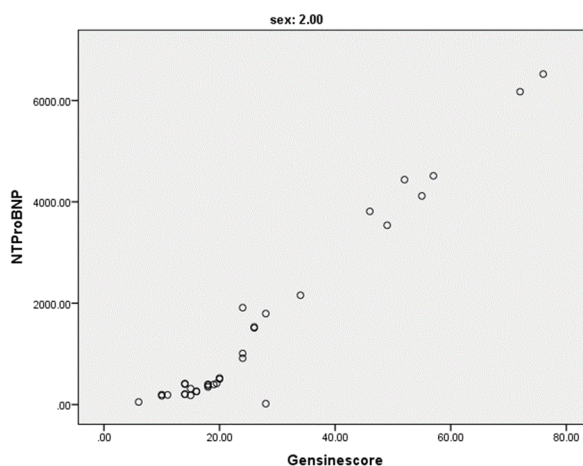
We tried to find any possible correlation between the serum level of NT-proBNP and Gensini score in our patients. Using Spearman's correlation test, the correlation coefficient was 0.953 ( $P < 0.001$ ), which showed a significant direct correlation between the two variables. The correlation was significant in both genders, as the Spearman's coefficients were 0.977 and 0.862 in males and females, respectively ( $P < 0.001$  in both). Fig 1-3 depict the correlation between serum levels of NT-proBNP and Gensini score in all the patients and each gender. Additionally, the correlation was significant in all three groups of patients with ACS (Table 2).

Group	Pearson's correlation coefficient	P value
UA	0.80	< 0.001
STEMI	0.96	< 0.001
NSTEMI	0.92	< 0.001

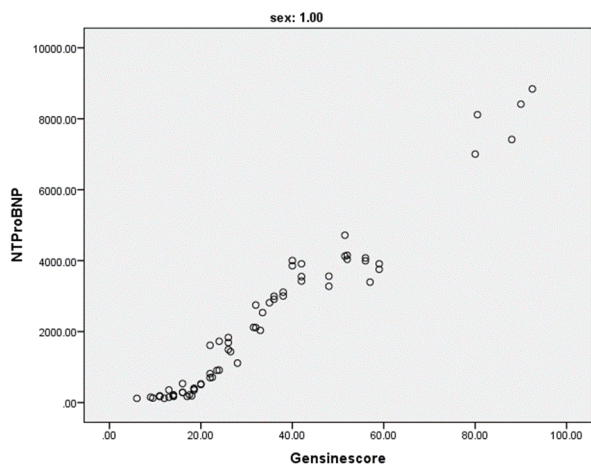
UA: unstable angina; STEMI: ST elevation myocardial infarction; NSTEMI: non-ST elevation myocardial infarction



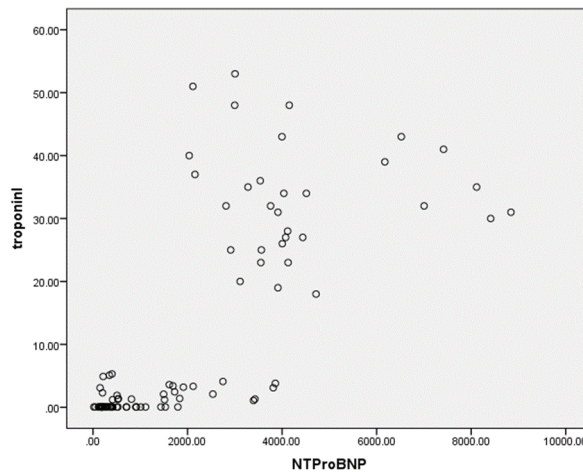
**Figure 1:** Correlation between Serum Levels of NT-proBNP and Gensini Scores in Patients



**Figure 3:** Correlation between Serum Levels of NT-proBNP and Gensini Scores in Females



**Figure 2:** Correlation between Serum Levels of NT-proBNP and Gensini Scores in Males



**Figure 4:** Correlation between Troponin I and NT-proBNP Levels

ANOVA showed no significant difference between serum levels of NT-proBNP among the four groups of patients with SVD, 2VD, 3VD and patients with isolated or concomitant LM involvement ( $P = 0.257$ ). Regarding the serum levels of NT-proBNP, there was also no significant difference between patients with and without LAD involvement ( $P = 0.294$ ). However, the difference was significant comparing patients with UA, STEMI and NSTEMI ( $P < 0.001$ ).

In this study, patients with positive troponin I had higher NT-proBNP levels ( $P < 0.001$ ) and the correlation coefficient between them was 0.779 (Fig 4). There was also a significant indirect correlation between serum level of NT-PRO-BNP and EF with a correlation coefficient of -0.55 ( $P = 0.001$ ).

Besides, while there was no significant difference in Gensini scores of smoker and non-smoker patients ( $P = 0.08$ ); smoker patients had higher NT-proBNP levels ( $P = 0.047$ ).

There was no correlation in Gensini scores and NT-proBNP levels with laboratory results of the patients (Tables 3 and 4).

**DISCUSSION**

In this study, we recruited patients with ACS and studied the correlation between their serum levels of NT-proBNP and Gensini scores. We found that the Spearman's coefficient of the correlation between serum levels of NT-proBNP and Gensini scores in our patients with ACS was 0.953 ( $P < 0.001$ ), which showed a powerful direct correlation between

**Table 3:** Correlation between Gensini Score and Laboratory Results

Variable	Correlation coefficient	P value
Blood sugar	0.1	0.73
HDL	-0.04	0.82
Triglyceride	0.003	0.34
LDL	0.086	0.76
Cholesterol	0.058	0.85

HDL: High-density lipoprotein; LDL: Low-density lipoprotein

**Table 4:** Correlation between Serum Level of NT-proBNP and Laboratory Results

Variable	Correlation coefficient	P value
Blood sugar	0.90	0.375
HDL	-0.021	0.839
Triglyceride	-0.014	0.893
LDL	0.029	0.773
Cholesterol	-0.002	0.987

HDL: High-density lipoprotein; LDL: Low-density lipoprotein

the two variables. The correlation was also statistically significant in both genders and in three subgroups of patients with UA, STEMI and NSTEMI. NT-proBNP was first used as an indicator of heart failure and stress on myocardial tissue; but it seems that it can also be considered as a valuable biomarker for predicting the severity of CAD and therefore the severity of myocardial ischemia.

The results of our study about the correlation between NT-proBNP and Gensini score are consistent with previous reports. Wei and colleagues reported that NT-proBNP levels were found to go higher with the severity of myocardial ischemia in patients with UA [26]. In a study on patients with NSTEMI, the NT-proBNP levels progressively increased with the severity of CAD, and increased levels of NT-proBNP independently predicted the presence of more complex coronary lesions [27]. Sahin Arslan and colleagues reported that plasma levels of BNP were higher in stable CAD patients with coronary artery stenosis of more than 50% compared to those with less stenosis; also, the level of increase in plasma BNP concentration was positively correlated with the extent of lesion on coronary angiography [16]. Some other studies have also found that the NT-proBNP level has been correlated with the severity of coronary artery stenosis and Gensini score and suggested that the NT-proBNP level can be used as a predictor of angiographic results [10, 20, 28].

Despite the significant correlation between NT-proBNP levels and Gensini scores in our patients, the NT-proBNP levels were not significantly different in patients with SVD, 2VD and 3VD ( $P = 0.257$ ). Inconsistent with our results, some studies have reported that NT-proBNP levels were positively correlated with the number of coronary vessels involved [10, 16]. However, individuals enrolled in those studies were patients with stable CAD. We also did not find any correlation between LAD involvement and NT-proBNP level; but in a study on patients with stable CAD [16] and another study on patients with UA and NSTEMI [29], patients with LAD involvement had higher NT-proBNP levels. Moreover, the results of our study showed that there was a direct correlation between NT-proBNP and troponin I levels (correlation coefficient = 0.779) in patients with ACS.

In addition to previous reports on higher NT-proBNP levels in patients with heart failure, we found that NT-proBNP levels had a negative correlation with EF in patients with ACS, too (correlation coefficient = -0.55;  $P = 0.001$ ). Some researchers have reported same results in patients with NSTEMI [27] and stable CAD [20].

Besides, while dyslipidemia and high blood sugar are risk factors of CAD; neither NT-proBNP levels nor Gensini scores were correlated with plasma levels of HDL, LDL, TG, cholesterol and blood sugar. Additionally, in contrast to Gensini score, smoker patients had higher NT-proBNP levels ( $P = 0.047$ ).

To conclude, serum levels of NT-proBNP can be used as an important biomarker for risk stratification of patients with ACS by predicting the CAD severity, Gensini score and troponin I levels. Further studies with higher numbers of patients are necessary to confirm the results of the current study.

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## CONFLICTS OF INTEREST

There is no conflict of interest for the authors.

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