Detection of severity of Acute Coronary Syndrome using N Terminal PRO-BNP and as a prognostic marker

Faheem Abd EL Azim Rageb[1]; Dalia Mohammed Rageb[1]; Ahmed Hossam Moafy[1]; Amr Mohammed Essmat[2]; Ahmed Fathy Mohammed Mahmoud[2]

[1]Critical care Medicine Department, Faculty of Medicine, Cairo University, Egypt.
[2]Critical care Medicine Department, Faculty of Medicine, Fayoum University, Egypt.
elkhateeb_ahmed@yahoo.com

Abstract: Background: Patients with unstable CAD encompass a heterogeneous group that varies widely regarding severity of the underlying coronary artery disease, prognosis and response to treatment. Patients with the highest risk of subsequent events usually have the largest benefit of an intensified pharmacological treatment and early mechanical intervention. Levels of natriuretic peptides have been shown to reflect cardiac performance and there is emerging role of these peptides in the early risk stratification of unstable CAD patients. Aim of the study: To study the prognostic value of natriuretic peptides in patients with acute coronary syndrome. Patients and methods: Seventy four patients were included in this study all patients included were subjected to History taking and full clinical assessment, Routine Laboratory investigation, Cardiac specific troponin I and CK-MB, Serum level of NT – pro BNPand Echocardiography for all patients for evaluation of both systolic and diastolic functions, Coronary angiography for detection of severity of affection of coronary vessel. Results: In our study N Terminal BNP was significantly higher in more sever coronary artery affection with p value 0.015, that there is a trend toward higher mortality with increasing levels of N terminal BNP and this trend was statistically significant with p value 0.025. Conclusion: Our study demonstrated that Serum N Terminal BNP can be used to detect severity of the lesion and follow up patients with CAD, significantly higher in more severe coronary artery affection and there is a higher mortality with its increasing levels

[Faheem Abd EL Azim Rageb; Dalia Mohammed Rageb; Ahmed Hossam Moafy; Amr Mohammed Essmat; Ahmed Fathy Mohammed Mahmoud. **Detection of severity of Acute Coronary Syndrome using N Terminal PRO-BNP and as a prognostic marker.** *J Am Sci* 2017;13(2):43-48]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 6. doi:10.7537/marsjas130217.06.

Key Words: Acute coronary syndrome, brain (B‐type) natriuretic, peptide (BNP), N‐terminal fragment of proBNP (NT‐proBNP).

1. Introduction

Acute coronary syndrome (ACS) refers to any group of symptoms attributed to obstruction of the coronary arteries. The most common symptom prompting diagnosis of ACS is chest pain, often radiating of the left arm or angle of the jaw, pressure-like in character, and associated with nausea and sweating. Acute coronary syndrome usually occurs as a result of one of three problems: ST elevation myocardial infarction (30%), non ST elevation myocardial infarction (25%), or unstable angina (38%)[1].

NT-Pro BNP in Acute coronary syndrome

The elevated serum level of NT-pro BNP in patients with left ventricular (LV) dysfunction and has shown a close correlation with the BNP level. Many reports have shown that the absolute increment of NT-pro BNP exceeded that of BNP, and that NT-pro BNP can be a more discerning marker for the detection and evaluation of cardiac dysfunction than BNP. [11] B-type natriuretic peptide (BNP) and NT-pro BNP can help to identify and accurately discriminated CHF from respiratory disease causes of dyspnea.[12, 13] NT-pro BNP measurements act as a guide to current treatments strategies, as well as novel strategies, in patients with acute myocardial infarction and as markers for the severity of heart failure. [14; 15] NT-pro BNP provides information that may be superior to clinical judgment for the diagnostic evaluation of the patient with possible HF. It is a surrogate biomarker for prognosis after STEMI that is closely associated with myocardial damage as assessed by contrast-enhanced Cardiac MRI. [16] It is also an independent predictor of survival in patients with hypertension and increased left ventricular mass. [17] CK-MB acts as a marker of cytosolic damage that reflects the area at risk and the resultant size of the infarction. Whereas Tn-I acts as a marker of myofibril damage and elevated in proportion to infarct size per se. The clinical spectrum of ACS consists of ST elevation (STE) myocardial infarction (MI) (STEMI) and non-ST elevation (NSTEMI) or unstable angina (UA), which are classified from the acute phase electrocardiography (ECG) changes and the development of myocardial necrosis. STEMI caused by acute total coronary occlusion, whereas NSTEMI is associated with vulnerable plaque and subocclusive thrombosis. [18] Hence, we evaluate the clinical utility

and early detection of myocardial ischemia is elevated in NSTE-ACS and the best time for treatment of disease by synthetic peptide molecule.

2. Patients and methods

We conducted a prospective case-control study including 74 patients with acute coronary syndrome in the general Critical care unit of Fayoum University Hospital from March 2013 to November 2014.

Inclusion criteria:

Patients with acute coronary syndrome diagnosed according to Braun Wald's classification, or acute MI (AMI) according to the redefined ESC/ACC Committee criteria.ie unstable angina was diagnosed when chest pain longer than 20 min duration occurred with or without ST segment depression of≥0.05 mV and/or T - wave inversion in two contiguous leads in the electrocardiogram. Diagnosis of non - ST segment elevation acute myocardial infarction was based on the above mentioned criteria plus increased levels of troponin I or CK - MB.ST segment elevation acute myocardial infarction was diagnosed when chest pain longer than 20 min duration occurred with ST segment elevation of ≥0.05 mV in two contiguous leads in the electrocardiogram [10].

Exclusion criteria:

1- Patients in whom cardiopulmonary resuscitation was performed.

2- Patients with serum creatinine level >2.0 mg/dl.

3- Overt pump failure (≥NYHA class II).

4- Onset of ischemic symptoms > 10 hours.

All patients included were subjected to the following

- History taking and full clinical assessment.
- Laboratory investigation: blood urea, serum creatinine, serum sodium, serum potassium levels, random blood sugar, complete blood count, liver functions tests and lipid profile on admission and follow up.
- Cardiac specific troponin I and CK-MB.
- Serum level of NT – pro BNP.
- Echocardiography for all patients for evaluation of both systolic and diastolic functions.
- Coronary angiography for detection of severity of affection of coronary vessel.

We measured N terminal pro BNP in plasma specimens obtained within 10 hours after onset of ischemic symptoms. Blood samples were obtained in EDTA containing tubes and were centrifuged and collected plasma was frozen at - 20C. BNP levels were quantified using competitive immunoassay method using radiolabeled tracers (RIA) according to the manufacture.

Seventy four patients were included in this study and divided into three groups:

Group I: Twenty four patients with ST segment elevation acute myocardial infarction.

-Group II: Thirty patients with non ST segment elevation acute myocardial infarction and unstable angina.

-Group III: The control group.

3. Results

Our study showed that there was no statistically significant difference between the study groups regarding age, sex and risk factors except for dyslipidemia which was highly significant (Table1). The most common complication was malignant arrhythmia which occurred in 50% of patients in group I versus 13.3 % of patients in group II which was statistically highly significant followed by heart failure affecting 33% of patients in group I versus 6% of in group II with p value <0.0001 which also was statistically highly significant. None of group III patients had these complication tables (2). Patients in group I had significantly higher LVEDD and LVESD compared to groups II and III also significantly lower % EF in group I compared to groups II and III with p value <0.0001 table(3). Patients in group I had significantly higher troponin I (9.59 ± 6.11 in group I vs 0.69 ±1.72 in group II and 0.03 ± 0.01 in group III, value <0.0001). N Terminal pro BNP was also significantly higher in group I (2186.13 ± 481.485 in group I vs. 1846.17 ± 513.37 in group II and 148.90 ± 33.35 in group III, P value <0.0001) Table (4). N Terminal pro BNP was the only biomarker that is significantly higher in more severe CAD affection (1859.28 ± 527.51 in one vessel vs. 2233.40 ± 418.26 in two vessel and 2472.33 ± 253.67 in three vessel affection p value 0.015) while Troponin I and CK MB were not significantly higher in more sever disease Table(5). Patients who developed arrhythmia had significantly higher Troponin I levels (10.45 ± 6.42 vs. 1.45 ± 3.44, P value<0.0001), significantly higher CK MB levels(141.63 ± 68.19 vs. 42.00 ± 63.24, P value <0.0001) and significantly higher N Terminal pro BNP levels (2286.56 ± 384.51 vs. 1280.09 ± 931.68, P value <0.0001Table (6). All patients who developed heart failure had significantly higher troponin I levels (11.16 ± 6.27 vs. 1.89 ± 4.08, p value <0.0001), significantly higher CK MB levels (160.17 ± 58.46 vs. 44.84 ± 64.13, P value <0.0001) and significantly higher N Terminal pro BNP levels (2337.00 ± 401.64 vs1335.26 ± 928.02, P value <0.0001 Table (7). Patients who died have significantly higher Troponin I, CKMB, N Terminal pro BNP Table (9).

Table 1: Characteristics of study groups

Variable	Group I (24)	Group II (30)	Group III (20)	*P*-value
Age (years)	54.92 ± 6.84	54.83 ± 7.62	53.85 ± 8.15	0.874
Sex: Female Male	 6 18	 12 18	 9 11	0.341
Smoking	18	16	8	0.058
HTN	13	21	9	0.191
DM	16	12	3	0.002
Dyslipidemia	19	16	3	<0.0001
FH of IHD	1	18	0	0.671

Table 2: complications among the study groups:

Variable	Group I (24)	Group II (30)	Group III (20)	*P* -value
Arrhythmia	**12 (50.0)**	**4 (13.3)**	**0 (0.0)**	**<0.0001 (HS)**
Mortality	**3 (12.5)**	**2 (6.7)**	**0 (0.0)**	**0.258 (NS)**
HF	**10 (33.3)**	**2 (6.7)**	**0 (0.0)**	**<0.0001 (HS)**
CV event	**1 (4.2)**	**0 (0.0)**	**0 (0.0)**	**0.348 (NS)**

Table 3: Echocardiographic features among study groups

Variable	Group I (24)	Group II (30)	Group III (20)	*P* -value
EDD (cm)	5.19 ± 0.36	4.88 ± 0.38	4.41 ± 0.14	<0.0001 (HS)
ESD (cm)	3.61 ± 0.31	3.4 ± 0.34	2.86 ± 0.18	<0.0001 (HS)
EF (%)	57.29 ± 5.57	59.90 ± 3.88	64.55 ± 2.93	<0.0001 (HS)

Table 4: Cardiac enzymes among study groups:

Variable	Group I (24)	Group II (30)	Group III (20)	*P* -value
Troponin I (ng/ml)	9.59 ± 6.11	0.69 ± 1.72	0.03 ± 0.01	<0.0001 (HS)
CK MB (U/L)	155.17 ± 64.23	23.60 ± 30.73	13.50 ± 5.14	<0.0001 (HS)
N term pro BNB (pg/ml)	2186.13 ± 481.485	1846.17 ± 513.37	148.90 ± 33.35	<0.0001 (HS)

Table 5: Cardiac enzymes and number of affected vessels:

Variable	One vessel (36)	Two vessels (15)	Three vessels (3)	*P* -value
Troponin I (ng/ml)	3.9 ± 4.99	7.04 ± 7.69	5.34 ± 9.23	0.186 (NS)
CK MB (U/L)	70.00 ± 74.24	111.40 ± 89.74	80.33 ± 120.96	0.260 (NS)
N term pro BNB (pg/ml)	1859.28 ± 527.51	2233.40 ± 418.26	2472.33 ± 253.67	0.015 (S)

Table 6: Cardiac enzymes in relation to malignant arrhythmia:

Variable	With arrhythmia (16)	Without arrhythmia (58)	*P* -value
Troponin I (ng/ml)	10.45 ± 6.42	1.45 ± 3.44	<0.0001 (HS)
CK mb (U/L)	141.63 ± 68.19	42.00 ± 63.24	<0.0001 (HS)
N term pro BNB (pg/ml)	2286.56 ± 384.51	1280.09 ± 931.68	<0.0001 (HS)

Table 7: Cardiac enzymes in relation to HF:

Variable	With HF(12)	Without HF(62)	*P* -value
Troponin I (ng/ml)	11.16 ± 6.27	1.89 ± 4.08	<0.0001 (HS)
CK mb(U/L)	160.17 ± 58.46	44.84 ± 64.13	<0.0001 (HS)
N term pro BNB (pg/ml)	2337.00 ± 401.64	1335.26 ± 928.02	<0.0001 (HS)

Table 9: Cardiac enzymes in relation to mortality:

Variable	Died (5)	Alive (69)	*P* -value
Troponin I (ng/ml)	10.96 ± 5.98	2.84 ± 5.22	0.001 (HS)
CK MB (U/L)	165.20 ± 42.54	56.17 ± 72.72	0.002 (HS)
N term pro BNB (pg/ml)	2122.60 ± 457.06	1452.42 ± 950.77	0.025 (S)

Table 10: Validity of cardiac enzymes as predictors for > one vessel affection:

tests	Cut off point	AUC	Sensitivity (%)	Specificity (%)	Overall accuracy (%)
Troponin I (ng/ml)	**1.45**	**0.609**	**61.1**	**55.5**	**57.4**
CK mb(U/L)	**21.00**	**0.604**	**66.7**	**55.5**	**59.2**
N term pro BNB (pg/ml)	**2051.50**	**0.710**	**77.8**	**63.9**	**68.5**

4. Discussion

Natriuretic peptides are vasoactive hormone secreted by the heart as part of a systemic response to cardiac stress and ventricular dysfunction.

Elevated BNP and NT pro BNP concentrations at admission in the setting of acute coronary syndrome (ACS) are associated with poor prognosis, including increased mortality, development of congestive heart failure (CHF), and recurrent ischemic events [11,12]. Because of its incremental prognostic value, NT-pro BNP assessment should be considered in clinical routine for risk stratification of patients with normal troponin [13]. NT-pro BNP can be a good parameter for predicting the severity of coronary vessels involvements alongside other diagnostic tools [14]. In the current study we performed a prospective observational study in a general intensive care unit (Fayoum University Hospital) on 74 patients newly admitted to ICU with acute coronary syndrome to study the prognostic value of natriuretic peptides in these patients and to evaluate the relationship between NT-pro BNP and severity of coronary vessels defects in Acute Coronary Syndrome patients.

In our study, analysis of the data showed that there was no statistically Significant difference among the study groups regarding age, sex, DM, hypertension, smoking but there was statistically significant difference.

Regarding dyslipidemia. vs. controls. The cholesterol level was elevated in79% of patients 0f group I (19 out of 24) versus 53% of patients of group II(16 out of 30), (*p* value <0.001), in contrast, the controls showed elevated cholesterol level in only 13% (3 out of 20). Similar findings observed by **Omland *et al.*** [15]**, and James *et al.*** [16].

In our study, analysis of the data showed that the most common.

complication was malignant arrhythmia which occurred in 50% of patients in group I versus 13.3 % of patients in group II which was statistically highly significant followed by heart failure affecting 33% of patients in group I versus 6% of in group II with *p* value <0.0001 which also was statistically highly significant. None of group III patients had these complications. Similar findings observed by **Shahabi *et al.***[14] and was also supported by **Emdin *et al.*** [17] who found that NT-pro BNP had acceptable accuracy for identifying heart failure due to left ventricular dysfunction [17]. Additionally, in the **Grewal *et al.***, study, [18]. BNP was identified as the strongest predictor of diastolic dysfunction as determined by Doppler-echocardiography. In our study, analysis of the data showed that Patients in group I had significantly higher LVEDD and LVESD compared to groups II and III also significantly lower % EF in group I compared to groups II and III with *p* value<0.0001.

In our study, analysis of the data showed that Patients in group I had Significantly higher troponin I (9.59 ± 6.11 in group I vs. 0.69 ± 1.72 in group II and 0.03 ± 0.01 in group III, value <0.0001). N Terminal pro BNP was also significantly higher in group I (2186.13 ± 481.485 in group I vs.1846.17 ± 513.37 in group II and 148.90 ± 33.35 in group III *P* value <0.0001. In our study, analysis of the data showed that N Terminal pro BNP was the only biomarker that is significantly higher in more severe CAD affection (1859.28 ± 527.51 in one vessel vs. 2233.40 ± 418.26 in two vessel and 2472.33 ± 253.67 in three vessel affection) *p* value 0.015 while Troponin I and CK MB were not significantly higher in more sever disease. These agree with the studies that focused on the association between the severity of CAD and NT-pro-BNP level [19-21] **Weber *et al.*** [19] Found that serum BNP level could effectively predict coronary involvement based on the number of affected coronary vessels in patients with angina pectoris. Also, **Sadanandan *et al.*** [20] showed that patients with BNP more than 80pg/ml had tighter culprit vessel stenosis and a higher number of culprit vessels compared to cases with lower plasma BNP level. Furthermore, **Hamishayev *et al.*** found a significant correlation between NT-proBNP levels and the number of affected vessels in patients with unstable angina and ST segment elevation MI [21].

In our study, analysis of the data showed that Patients who developed Arrhythmia had significantly higher Troponin I levels (10.45 ± 6.42 vs. 1.45± 3.44 *P* value<0.0001), significantly higher CK MB levels (141.63 ± 68.19vs. 42.00 ± 63.24 *P* value <0.0001) and significantly higher N Terminal proBNP levels (2286.56 ± 384.51 vs. 1280.09 ± 931.68 *P* value <0.0001. In our study, analysis of the data showed that all patients who Developed heart failure had

significantly higher troponin I levels (11.16 ± 6.27 vs. 1.89 ± 4.08 *p* value <0.0001), significantly higher CK MB levels (160.17 ± 58.46 vs. 44.84 ± 64.13 *p* value <0.0001) and significantly higher Terminal pro BNP levels (2337.00 ± 401.64 vs1335.26 ± 928.02 *p* value< 0.0001. In our study, analysis of the data showed that Patients who died has significantly higher Troponin I, CKMB, N Terminal pro BNP (2122 ± 457 in patients who died vs. 1452.5± 950.7 in In patients who alive) *p* value0.025. These agrees with the studies conducted by **Morita, Yasue, *et al*.**,[22] **Talwar, Squire, *et al*.** [23]. And **Omland, Aakvaag, *et al*.** [15][24] Together, these studies provide consistent evidence for the additive prognostic value of BNP. Moreover, whether measured at presentation or later during recovery, BNP is one of the most robust indicators of mortality risk **Mega, Morrow, *et al*.** [25,26].

Conclusion

Our study demonstrated that Serum N Terminal BNP can be used as a biomarker to detect severity of the lesion and follow up patients with CAD. In our study N Terminal BNP was the only biomarker that is significantly higher in more sever coronary artery affection with p value 0.015. while CKMB and Troponin I were not. Our study found that there is a trend toward higher mortality with increasing levels of N terminal BNP and this trend was statistically significant.

References

1. Torres M, Moayedi S (May 2007). "Evaluation of the acutely dyspneic elderly patient". Clin. Geriatr. Med. 23 (2): 307–25, VI. doi:10.1016/j.cger.2007.01.007. PMID 17462519.
2. Seino Y, Ogawa A, Yamashita T, Fukushima M, Ogata K, Fukumoto H, TakanoT. Application of NT-pro BNP and BNP measurements in cardiac care: A morediscerning marker for the detection and evaluation of heart failure. Eur J HeartFail. 2004;6:295– 300. [PubMed]
3. van der Burg-de Graauw N, Cobbaert CM, Middelhoff CJ, Bantje TA, van Guldener C. The additive value of N-terminal pro-B-type natriuretic peptide testing at the emergency department in patients with acute dyspnoea. Eur J Intern Med. 2009;20:301–6. [PubMed]
4. Fox PR, Oyama MA, Reynolds C, Rush JE, Defrancesco TC, Keene BW, Atkins CE, Macdonald KA, Schober KE, Bonagura JD, Stepien RL, Kellihan HB, Nguyenba TP, Lehmkuhl LB, Lefbom BK, Moise NS, Hogan DF. Utility of plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) to distinguish between congestive heart failure and non-cardiac causes of acute dyspnea in cats. J vet cardiol. 2009;23:51–61. [PubMed]
5. Lorgis L, Zeller M, Dentan G, Sicard P, Buffet P, L'Huillier I, Beer JC, Vincent-Martin M, Makki H, Gambert P, Cottin Y. RICO Survey Working Group. Prognostic value of N-terminal pro-brain natriuretic peptide in elderly people with acute myocardial infarction: prospective observational study. BMJ. 2009;6; 338:b1605. [PMC free article] [PubMed]
6. Heringlake M, Kox T, Poeling J, Klaus S, Hanke T, Franz N, Eberhardt F, Heinze H, Armbruster FP, Bahlmann L. The effects of physical exercise on plasma levels of relaxin, NTproANP, and NTproBNP in patients with ischemic heart disease. Eur J Med Res. 2009;14:106–12. [PMC free article] [PubMed]
7. Bruder O, Jensen C, Jochims M, Farazandeh M, Barkhausen J, Schlosser T, Sabin GV, Hunold P. Relation of B-type natriuretic peptide (BNP) and infarct size as assessed by contrast-enhanced MRI. Int J Cardiol. 2009;144:53–58. [PubMed]
8. Garcia S, Akbar MS, Ali SS, Kamdar F, Tsai MY, Duprez DA. N-terminal pro B-type natriuretic peptide predicts mortality in patients with left ventricular hypertrophy. Int J Cardiol. 2009;143:349–352. [PubMed]
9. Alpert J, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined: A consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am CollCardiol. 2000;36:959– 969. [PubMed].
10. E. Braun Wald, E. Antman, J. Beasley, R. M. Califf, M. D. Cheitlin, J. S. Hochman, R. H. Jones, D. Kereiakes, *et al.,* "ACC/AHA Guidelines for the Management of Patients with Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina)," Journal of the American College of Cardiology, Vol. 36, No. 3, 2000, pp. 970-1062.
11. Morita E, Yasue H, Yoshimura M, Ogawa H, Jougasaki M, Matsumura T, *et al.*. Increased plasma levels of brain natriuretic peptide in patients with acute myocardial infarction. Circulation 1993;88(1):82–91.
12. Morrow DA, de Lemos JA, Blazing MA, Sabatine MS, Murphy SA, Jarolim P, *et al.*. Prognostic value of serial Btype natriuretic peptide testing during follow-up of patients with

unstable coronary artery disease. JAMA2005; 294(22):2866–71.
13. Weber M, Bazzino O, Navarro Estrada JL, Fuselli JJ, BottoF, Perez de Arenaza D, *et al.*. N-terminal B-type natriuretic peptide assessment provides incremental prognostic confirmation in patients with acute coronary syndromes and normal troponin T values upon admission Am Coll Cardiol. 2008; 51(12). 1188–95.
14. Shahabi V, Moazenzadeh M, Azimzadeh BS, NasriH, Afshar RM, Shahesmaili A, *et al.*. Relationship between serum N-termina pro brain natriuretic peptide (NTproBNP) level and the severity of coronary artery involvements. J Res Med Sci 2011; 16(2):143–8.
15. Omland T, Aakvaag A, Bonarjee VV *et al.* Plasma brain natriuretic peptide as an indicator of left ventricular systolic function and long‐term survival after acute myocardial infarction. Comparison with plasma atrial natriuretic peptide and N‐terminal pro atrial natriuretic peptide. Circulation1996; 93:1963 – 9.
16. James SK, Lindahl B, Siegbahn A, *et al.* N‐terminal pro‐brain natriuretic peptide and other risk markers or the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open occluded arteries (GUSTO)‐IV sub‐study. Circulatio2003; 108:275–281.
17. Emdin M, Passino C, Prontera C, Fontana M, PolettiR, Gabutti A, *et al.* Comparison of brain natriuretic peptide (BNP) and amino-terminal Pro BNP for early diagnosis of heart failure. ClinChem 2007; 53(7):1289–97.
18. Grewal J, McKelvie R, Lonn E, Tait P, Carlsson J, Gianni M, *et al.*. BNP and NT-pro BNP predict echocardiographic severity of diastolic dysfunction. Eur J Heart Fail 2008; 10(3):252–9.
19. Weber M, Dill T, Arnold R, Rau M, Ekinci O, Müller KD, *et al.*. N-terminal Btype natriuretic peptide predicts extent of coronary artery disease and ischemia in patients with stable angina pectoris. Am Heart J2004; 148(4):612–20.
20. Sadanandan S, Cannon CP, Chekuri K, Murphy SA, Dibattiste PM, Morrow DA, *et al.*. Association of elevated B-type natriuretic peptide levels with angiographic findings among patients with unstable angina and nonST-segment elevation myocardial infarction. J Am CollCardiol 2004;44(3):5648.
21. Hamishayev JZ. Can NT-proBNP together with Doppler tissue imaging predict severity of coronary artery disease in patients with acute coronary syndrome? Atherosclerosis Suppl 2008; 9(1):174–5.
22. Morita E, Yasue H, Yoshimura M, Ogawa H, JougasakiM, Matsumura T, *et al.* Increased plasma levels of brain natriuretic peptide in patients with acute myocardial infarction. Circulation 1993; 88(1):82–91.
23. Talwar S, Squire IB, Downie PF, Mccullough AM, Campton MC, Davies JE, *et al.* Profile of plasma N terminal pro BNP following acute myocardial infarction; correlation with left ventricular systolic dysfunction. Eur Heart J 2000;21(18):1514–21.
24. Presentation with unstable angina or non‐ST‐elevation myocardial infarction: results from OPUS‐TIMI16 and TACTICS‐TIMI 18. Am Heart J 2004; 148:173–180.
25. Mega JL, Morrow DA, de Lemos JA, Sabatine MS, MurphySA, Rifai N, *et al.* B-type natriuretic peptide at presentation and prognosis in patients with STsegment elevation myocardial infarction: an ENTIRE–TIMI-23 substudy. J Am CollCardiol. 2004; 44(2):335–9.
26. Morrow DA, de Lemos JA, Sabatine MS, Murphy SA Demopoulos LA, Di Battiste PM, *et al.* Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/non-ST-elevation myocardial infarction: B-type natriuretic peptide and prognosis in TACTICS-TIMI183-Shahabi V, Moazenzadeh M, Azimzadeh BS, NasriH, Afshar RM, Shahesmaili A, *et al.* Relationship between serum N-termina pro brain natriuretic peptide(NTproBNP) level and the severity of coronary artery involvements. J Res Med Sci 2011; 16(2):143–8.

1/25/2017