

# Correlation of Cardiac Markers NT-Pro BNP (N-terminal Fragment of B-type Natriuretic Peptide) and cTI (Cardiac Troponin I) in Acute Coronary Syndrome, Ventricular Dysfunction, Myocardial Ischemia And Necrosis.

Shazia Noureen, \*Junaid Mahmood Alam, Howrah Ali, Aijaz Ahmed, Ishrat Sultana

Department of Biochemistry Laboratory Services and Chemical Pathology,  
Liaquat National Hospital and Medical College, Karachi. Pakistan.

(\*Corresponding author; Dr Junaid Mahmood Alam, dr\_jmalam@hotmail.com)

## 1. Abstract

**Background:** Diagnostic efficacy of cardiac markers, N-terminal fragment of Pro-BNP (NT-Pro BNP) and Troponin I (cTI) has long been known as significant predictor of survival and mortality in cardiac patients. **Aim:** The present study was undertaken to demonstrate significance and correlation of NT-pro BNP and cTI in cardiac anomalies to suggest diagnostic importance of both or either markers in selected population of male and female cardiac patients. **Materials and Methods:** Two hundred and thirty patients (males = 104; females = 126, age range = 21-90 yrs) with either chest pain, dyspnea or with known history of acute coronary syndrome, Ischemic stroke, ventricular dysfunction or myocardial infarction/ necrosis were included in this retrospect observational study from 21<sup>st</sup> October 2013 to 16<sup>th</sup> November 2014. The patients were divided into four groups G, I, II, III and IV according to none or elevation of both or either cardiac markers. Plasma was analyzed for NT-pro BNP and cTI on Elecsys 2010; Cobas e411 and Cobas e601 using electro-chemi luminescence (ECLi) immunoassay technology (Roche Diagnostics, Basil). **Results:** Collected and measured data showed that 48.07% (n = 50) of male patients showed elevated levels of both NT-pro-BNP and cTI (Group I) whereas individually elevated NT-pro BNP (group II) was manifested in 50% patients (n = 52). In female group of patients, 42.85% (Group I, n = 54) exhibited elevated NT pro-BNP and cTI, whereas 49.20% (Group II, n = 62) manifested elevated NT pro-BNP and normal cTI. Comparison amongst group I and II in both gender although showed non significance between groups with elevation of both cardiac markers and NT pro-BNP only, but still, percent wise diagnostic efficacy and onset of both cardiac markers in group I is considerably vigorous when compared with groups II, III and IV. **Conclusion:** In conclusion, combined elevation of both NT pro-BNP and cTI in cardiac patients suggests poor prognosis and urgent follow-up with immediate medical care.

**Key words:** N-terminal fragment of Pro-BNP (NT-Pro BNP), Troponin I (cTI), acute coronary syndrome (ACS), Ischemic stroke, ventricular dysfunction or myocardial infarction (MI) or necrosis.

## 2. Introduction

Pro BNP (B-type Natriuretic peptide) is a cardiac neuro-hormone whereas Troponin I (cTI) is a regulatory protein of cardiac origin [1]. The N-terminal fragment of Pro-BNP (NT-Pro BNP) is

synthesized in myocardial ventricular part [2,3]. Both NT-pro BNP and cTI cardiac markers are known to be

elevated in patients with acute coronary syndrome (ACS), ventricular dysfunction, and /or myocardial ischemia/necrosis, respectively [1,4-6]. Diagnostic efficacy of both cardiac markers has long been known as significant predictor of survival and mortality [7-9]. Furthermore, comparative studies on the efficacy or significance of both makers, simultaneously in ACS, Ischemic stroke or myocardial necrotic patients, have been reported earlier [1,10-12]. In present study, we demonstrated significance and correlation of NT-pro BNP and cTI in cardiac anomalies to suggest diagnostic importance of both or either markers in selected population of male and female cardiac patients.

## 3. Materials and Methods

**Patients' selection and study design:** Two hundred and thirty patients (males = 104; females = 126, age range = 21-90 yrs) with either chest pain, dyspnea or with known history of ACS, Ischemic stroke, ventricular dysfunction or myocardial infarction/ necrosis were included in this retrospect observational study from 21/10 2013 to 16/11/2014. The inclusion criteria were clinical symptoms or known history of ACS, Ischemic stroke, ventricular dysfunction or myocardial infarction and necrosis. The patients who are on steroid therapy, underwent surgery, suffering from renal impairment were excluded from the study.

### **Measurement of cardiac Troponin I and NT-pro BNP:**

Blood samples were collected from 230 patients in heparinized tubes. The patients were divided into four groups according to none or elevation of both or either cardiac markers, NT-pro BNP and cTI. Group I = NT-pro BNP ↑ and cTI ↑; group II = NT-pro BNP ↑ and cTI ↔; Group III = NT-pro BNP ↔ and cTI ↔ and group IV = NT-pro BNP ↔ and cTI ↑. (↔ = normal levels, ↑ = elevated levels). Plasma was separated and analyzed for NT-pro BNP and cTI on Elecsys 2010; Cobas e411 and Cobas e601 using electro-chemi luminescence (ECLi) immunoassay technology (Roche Diagnostics, Basil). Normal reference range of cTI = < 0.30 ng/ml, NT-pro-BNP = males < 100 pg/ml, females = <150 pg/ml. The data was compared statistically by using SPSS ver 13.0 (USA) and considered significant when P < 0.05.

#### 4. Results

The results are summarized in tables 1 and 2. Around two hundred and thirty patients, both males (n = 104) and females (n = 126) were included in present study. All patients were diagnosed with or shown clinical symptoms of ACS, Ischemic stroke, ventricular dysfunction or myocardial infarction and necrosis. Collected and measured data showed that 48.07% (n = 50) of male patients showed elevated levels of both NT-pro-BNP and cTI (Group I) whereas individually elevated NT-pro BNP (group II) was manifested in 50% patients (n = 52) [Table 1]. Only one patient each in Group III and IV were categorized according to normal NT pro-BNP and cTI and normal NT pro BNP and elevated cTI, respectively. Similarly in female group of 126 patients, most of them were found to be suffering from MI, myocardial necrosis, ACS and Ischemia. Around forty two percent (42.85%) patients (Group I, n = 54) exhibited elevated NT pro-BNP and cTI, whereas 49.20% (Group II, n = 62) manifested elevated NT pro-BNP and normal cTI [Table 2]. Furthermore, 5.55% (group III, n = 7) exhibited normal levels of both NT pro-BNP and cTI, whereas 2.30% patients (group IV, n = 3) manifested normal NT pro BNP and elevated cTI [Table 2]. Mean values of NT pro-BNP and cTI in male patients' groups ranged from 4819.25 ± 36.28 pg/ml to 28.40 pg/ml and 12.29 ± 4.25 ng/ml to 0.09 ng/ml, respectively (Table 1). Similarly, in female patients' group mean values of NT pro-BNP and cTI ranged from 3201.75 ± 41.50 pg/ml to 39.26 ± 1.28 pg/ml and 10.96 ± 2.50 ng/ml to 0.09 ± 0.01 ng/ml, respectively (Table 2). Comparison amongst group I and II in both gender although showed non-significance between groups with elevation of both cardiac markers and NT pro-BNP only, but still, percent wise efficacy of both cardiac markers in group I is considerably vigorous when compared with groups II, III and IV.

**Table 1: Determination of levels of NT-pro BNP and cTI in male cardiac patients (n = 104)**

Groups	Number of patients	NT-pro BNP (pg/ml)	cTI (ng/ml)	Percentage per group w.r.t. total patients
Group I	50	4819.25 ± 36.28	12.29 ± 4.25	48.07%
Group II	52	1826.35 ± 40.40	0.100 ± 0.001	50.00%
Group III	01	28.40	0.09	0.96%
Group IV	01	54.60	5.98	0.96%

[w.r.t. = with respect to]

**Table 2: Determination of levels of NT-pro BNP and cTI in female cardiac patients (n = 126)**

Groups	Number of patients	NT-pro BNP (pg/ml)	cTI (ng/ml)	Percentage per group w.r.t. total patients
Group I	54	3201.75 ± 41.50	10.96 ± 2.50	42.85%
Group II	62	1426.20 ± 39.40	0.12 ± 0.02	49.20%
Group III	07	39.26 ± 1.28	0.09 ± 0.01	5.55%
Group IV	03	46.70 ± 2.10	6.96 ± 2.10	2.30%

#### 5. Discussion

Present study described the diagnostic efficacy of NT pro-BNP and cTI in patients with ACS, MI, myocardial necrosis, ventricular dysfunction, stroke, and Ischemia in both male and female groups. The data exhibited considerable percentage, more than 40% in both gender that manifested elevated levels of NT pro-BNP and cTI in several forms of cardiac anomalies. A study reported earlier [11] also showed similar pattern of diagnostic utility and manifestation of NT pro-BNP and cTI in patients attending accident and emergency department with suspected cardiac episodes. The group also suggests that levels of NT pro-BNP above 60.00 pg/ml were an independent factor for supra-ventricular tachyarrhythmia (SVT) [11]. Furthermore, elevation of cTI in cardiac episode is well documented, especially in tachyarrhythmia [13-15].

It was emphasized in several previous studies that cardiac markers such as NT pro-BNP and cTI are useful independent indicators or combo-factors for the prediction of proceeding cardiovascular anomalies [1]. Cohort studies done earlier reported combined and independent prognostic significance of NT pro-BNP and cardiac Troponins in myocardial infarctions [16-18]. The report suggested that cardiac patients were at high risk of fatality within 3 days of follow-ups, if several or both (tropinins and NT pro-BNP) cardiac markers were found elevated [17,18].

#### 6. Conclusion:

Present study described the significance of cardiac markers, NT pro-BNP and cardiac Troponin I in patients with cardiac anomalies such as ACS, MI, ventricular dysfunction, myocardial necrosis and Ischemia. The combined elevation of both NT pro-BNP and cTI in cardiac patients suggests poor prognosis and urgent follow-up with immediate medical care.

#### 7. References

- [1]. Zdravkovic V, Mladenovic V, Colic M, Bankovic D, Lazic Z, Petrobic M, Simic I, Kenezovic S, Pantovic S, Djukic A, Zdravkovic N. NT-proBNP for prognostic and diagnostic evaluation in patients with acute coronary syndromes. *Kardiologia Polska* 2013; 71 (5): 472-479.
- [2]. Mantymaa P, Vuolteenaho O, Marttila M et al. Atrial stretch induces rapid increase in brain natriuretic peptide but not in atrial natriuretic peptide gene expression in vitro. *Endocrinology*, 1993; 133: 1470-1473.
- [3]. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. *N Engl J Med*, 1998; 339: 321-328.
- [4]. Goetze JP, Christoffersen C, Perko M et al. Increased cardiac BNP expression associated with myocardial ischemia *FASEB J*, 2003; 17: 1105-1107.
- [5]. Hall C. Essential biochemistry and physiology of (NT-pro) BNP. *Eur J Heart Fail*, 2004; 6: 257-260.
- [6]. Apple FS. Cardiac troponin I. In: Wu AHB ed. *Pathology and laboratory medicine: cardiac markers*. Humana Press Inc/USA, New York 1998: 229-243.
- [7]. Morrow DA, de Lemos JA, Sabatine MS 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-TIMI 18. *J Am Coll Cardiol*, 2003; 41: 1264–1272.
- [8]. Omland T, de Lemos JA, Morrow DA, Antman EM, Cannon CP, Hall C, Braunwald E. Prognostic value of N-terminal pro-atrial and pro-brain natriuretic peptide in patients with acute coronary syndromes. *Am J Cardiol*, 2002; 89: 463–465.
- [9]. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Engl J Med*, 1996; 335: 1342–1349.
- [10]. Etgen T, Baum H, Sander K, Sander D. Cardiac troponins and N-terminal pro-brain natriuretic peptide in acute ischemic stroke do not relate to clinical prognosis. *Stroke*. 2005;36(2):270-5
- [11]. Ocak T, Erdem A, Duran A, Tekelioglu UY, Tekelioglu ÜY, Öztürk S, Ayhan SS, Özlü MF, Tosun M, Koçoğlu H, Yazıcı M. The diagnostic significance of NT-proBNP and troponin I in emergency department patients presenting with palpitations. *Clinics (Sao Paulo)*. 2013; 68(4):543-7
- [12]. Nassar Y, Monsef D, Abdelshafy S, Hamed G. NT-proBNP, troponin I and troponin T are elevated in ARDS patients without structural heart disease: a single initial reading of cardiac markers is not different from serial daily readings. *Critical Care* 2011, 15 (Suppl 1):P131
- [13]. Zellweger MJ, Schaer BA, Cron TA, Pfisterer ME, Osswald S. Elevated troponin levels in absence of coronary artery disease after supraventricular tachycardia. *Swiss Med Wkly*. 2003; 133(31-32):439-41.
- [14]. Redfearn DP, Ratib K, Marshall HJ, Griffith MJ. Supraventricular tachycardia promotes release of troponin I in patients with normal coronary arteries. *Int J Cardiol*. 2005;102(3):521-2
- [15]. Palazzuoli A, Caputo M, Calabro A, Nuti R. Clinical impact of BNP and other emerging biomarkers in heart failure evaluation and management. *Minerva Cardioangiol*. 2012;60(2):183-94.
- [16]. Westerhout CM, Fu Y, Lauer MS, James S, Armstrong PW, Al-Hattab E, Califf RM, Simoons ML, Wallentin L, Boersma E; GUSTO-IV . Short- and long-term risk stratification in acute coronary syndromes: the added value of quantitative ST-segment depression and multiple biomarkers. *J Am Coll Cardiol*, 2006; 48: 939–947.
- [17]. James SK, Lindbäck J, Tilly J, Siegbahn A, Venge P, Armstrong P, Califf R, Simoons ML, Wallentin L, Lindahl B. Troponin-T and N-terminal pro-B-type natriuretic peptide predict mortality benefit from coronary revascularization in acute coronary syndromes: a GUSTO-IV substudy. *J Am Coll Cardiol*, 2006; 48: 1146–1154.
- [18]. Daniels LB, Laughlin GA, Clopton P, Maisel AS, Barrett-Connor E. Minimally elevated cardiac troponin T and elevated N-terminal pro-B-type natriuretic peptide predict mortality in older adults: results from the Rancho Bernardo Study. *J Am Coll Cardiol*, 2008; 52: 450–459.