ORIGINAL ARTICLE

COMPARISON BETWEEN THE LEVELS OF N TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE AND TROPONIN I TO PREDICT LEFT VENTRICULAR EJECTION FRACTION IN PATIENTS PRESENTING WITH FIRST ST-ELEVATION MYOCARDIAL INFARCTION

Kaleem Ullah Sheikh[1], Amna Farooq[1], Abeer Sarfaraz[1], Sana Sarfaraz[2], Sadaf Athar[1], Aemon Zehra[1]

[1]Liaquat National Hospital, Karachi, Pakistan, [2]University of Karachi, Department of Pharmacy, Karachi, Pakistan

Objectives: To compare the levels of N Terminal- ProBrain natriuretic peptide (NT-proBNP) and Troponin I (Trop I) to predict left ventricular ejection fraction (LVEF) in patients presenting with first ST-elevation myocardial infarction (STEMI).

Methodology: A cross-sectional study was carried out in Cardiology department of a tertiary care hospital from June to November 2021. A total of 150 patients who presented at emergency department with first STEMI and underwent primary percutaneous coronary intervention (PCI) were included. The patient's second set of troponin I and NT-proBNP were collected during hospitalization. Echocardiography was done. Left ventricular function was assessed using modified Simpson's method. For data analysis, SPSS 21 was used.

Results: The mean age was 60.60±11.1 years. There were 76% males, 53% hypertensive, 44% diabetic, 14% smokers with the most prominent type of myocardial infarction being anterior wall myocardial infarction accounting for 76.7%. Mean Trop I was 12.2±6.81 ng/ml, 9.5±8.63 ng/ml and 3.0±5.41 ng/ml for LVEF≤40%, 41-49% and >50% respectively while NT-proBNP was 7136.4±7.97pmol/l, 2328.9±3498.6pmol/l and 441±283.6pmol/l for LVEF ≤40%, 41-49%, and >50% respectively. We found a significant mean difference for Trop I (p=0.000) and NT-proBNP (p=0.0001). There was an inverse significant relationship of left ventricular ejection fraction with Trop I (r=-0.290, p=0.000) and NT- proBNP (r=-0.388, p=0.000).

Conclusion: In comparison to Troponin I, NT-proBNP serves as a better marker to predict LVEF in patients presenting with first STEMI.

Keywords: NT Pro-BNP (N terminal Pro Brain natriuretic peptide), AMI (acute myocardial infarction), Trop I (Troponin I), STEMI (ST-elevation myocardial infarction)

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INTRODUCTION

One of the major causes of heart disease and one of the main causes of death worldwide is coronary artery disease. Additionally, it ranks as the leading global cause of early death.[1] An estimated 200,000 and 550,000 people per year are predicted to have a new or recurrent myocardial infarction, respectively. An acute myocardial infarction occurs in one American every 42 seconds, according to estimates. Acute ST-Elevation Myocardial Infarction, one of the illnesses with the highest rates of morbidity and mortality, is one of the most common cardiac crises. The best method for predicting death after an AMI is left ventricular function. The identification of cardiac biomarkers is a crucial step in the detection of ischemia and the estimate of infarct size.[2] the degree of irreversible myocardial damage is the element that best predicts a patient's prognosis following an AMI. When compared to creatine kinase—MB (CK-MB), the cardiac troponin I (cTnI) exhibits exceptional specificity and sensitivity, making it a superior diagnostic marker of myocardial necrosis. Because of its specific location in the myocardium and strong association between infarct size and release, cardiac troponin exhibits an inverse connection with left ventricular ejection fraction.[3]

It is acknowledged that certain cardiac enzymes, such as troponin and brain natriuretic peptide (BNP and NT-proBNP), are crucial for the diagnosis of heart disease.[3] Myocardial damage and myocardial infarction are indicated by increased troponin levels.[4]

a negative or low value for plasma NT-proBNP can rule out heart failure.

In numerous studies including elderly patients, it was found that there was a substantial association between Left Ventricular Ejection Fraction and NT-proBNP levels, demonstrating that reduced LVEF had an inverse relationship with NT-proBNP levels. Additionally, it has also been shown that left ventricular ejection fraction has an inverse relationship with another biomarker, Troponin-I, a potent marker of myocardial necrosis, particularly after the first AMI.[5]

The aim of this study was to compare the two biomarkers namely NT-proBNP and Trop I in predicting the left ventricular ejection fraction in patients who presented with first St elevation myocardial infarction. Since a lot of work has already been done on each individually and no comparison in this regard has been made previously hence in the study, we carried this out.

METHODOLOGY

A cross-sectional study was carried out at the cardiology department of a tertiary care hospital (Liaquat National Hospital) from June to November 2021. Informed consent was taken from the patients after approval of the ethical committee of the hospital. A sample size of 150 patients was calculated with the help of an online sample calculator. The inclusion criteria included both genders male and female with ages from 18 to 80 years who presented in the emergency department with first STEMI which was defined on the electrocardiogram as typical ST segment elevation >1mm in at least 2 or more contiguous leads. The patients presented with a characteristic chest pain lasting for more than 20 minutes but less than 24 hours at the time of arrival in the emergency department. Only COVID PCR negative patients were included in the study. The patients excluded from the study were those with renal failure, with surgical history (having cardiopulmonary bypass) or having any valve surgery or any valvular disease, those with a previous history of AMI, electrocardiograms with pre-existing bundle branch block or displaying non-sinus rhythm and poor quality echocardiographic images. The ECG of the patient was performed within 10 minutes of arrival in the emergency department. Emergency medical treatment was given which included Tablet Disprin 300mg per oral route, Tab Clopidogrel 600mg per oral route and Injection Heparin 70-100 Units/Kg via intravenous route and all patients underwent primary PCI.

A commercially available immunoassay (Roche Diagnostics) on an Elecsys 1010 Analyzer was used for the quantification of NT-Pro BNP according to established methods, the assay range being 5 – 35,000 pg/ml with normal values <194pg/ml. It was collected 12 hours after the first presentation.

Troponin I levels were measured using third generation immune histochemical assay (Elecys 1010, Roche Diagnostics), with detection range values 0.010-25.00ng/ml) and with values for MI >0.30ng/ml (sensitivity 100% and specificity 83.9% for first 24 hours) at presentation and after 12 hours. Echocardiographic- Doppler study was performed before discharge with 2.5-MHz transducers and LV function was assessed using the modified Simpsons method. The Echo was performed by the staff technician and reported by the staff Cardiologist, the treating Cardiologist was not involved in Echo reporting to prevent bias. The echocardiographic measurements were taken according to American Society of Echocardiography guidelines. Patients were divided into three groups according to their LV function. Those with LVEF (≤40%) were included in the reduced EF group (rEF), those with LVEF (41-49%) were included in the mildly reduced EF (mrEF) group and those with EF (50% and above) were included in preserved EF (pEF) group.

The clinical characteristics of each patient were recorded after the process of enrollment was completed. They included demographics, symptoms, signs, medical history, and co-morbidities (Diabetes, Hypertension, Dyslipidemia, smoking, family history of cardiovascular diseases). Statistical package for social sciences (SPSS) 21 was used for performing statistical analysis. Frequency and percentages were reported for categorical variables such as gender, diabetes, hypertension, smoking, and type of myocardial infarction. Descriptive analysis was used for age and for estimating the mean of both Trop I and NT Pro BNP for different categories of LV function. Mean comparison was done by one way ANOVA and post hoc tuckey test was applied. ROC Curve was used to illustrate and evaluate the diagnostic (prognostic) performance of NT-proBNP and Tropnin I. P value of < 0.05 will be considered as significant. LVEF was categorized into two categories LVEF<50 and LVEF≥50 and then ROC curve was applied for NT-proBNP and Troponin I.

RESULTS

Demographic and clinical details of the patients are shown in table 1. The mean age of the patients included was 60.60 ± 11.1 years out of which114 (76 %) were male. Out of the total patients, 80 (53.3%)

were hypertensive, 66 (44%) were diabetic, and 21 (14%) patients were smokers. In terms of the type of myocardial infarction encountered anterior wall was most common 76.7% (115), with anterolateral accounting for 10% (15), and inferior 13.3% (20).

Table 1: Demographic characteristics of study population

Patient's characteristics	Mean± S.D
Age (in years)	60.60 ± 11.1
Male	114 (76%)
Co-morbidities	
Hypertensive	80 (53%)
Diabetes	66 (44%)
Smokers	21 (14%)
Type of myocardial infarction	
Anterior wall	115 (76.7%)
Anterolateral wall	15 (10%)
Inferior	20 (13.3%)

SD; Standard Deviation

Trop I levels of greater than or equal to 25ng/ml predicted an LVEF of less than 40% whereas NT-proBNP levels of greater than or equal to 1000pg/ml predicted an LVEF of less than 40%. Although both cardiac biomarkers can help in predicting LVEF, NT-proBNP shows superiority with significant inverse correlation with Trop I (r=-0.290, p=0.000) and NT-proBNP (r=-0.388, p=0.000) (Figure 1).

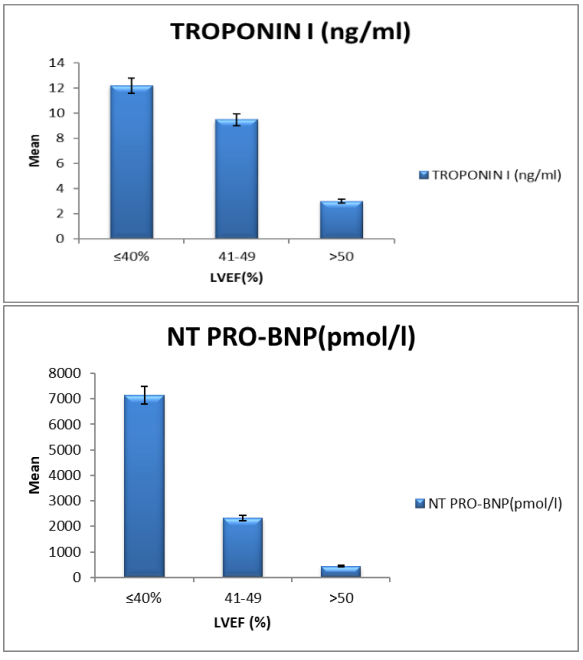

Figure 1: (a): Mean valves of Troponin I in correlation with LVEF (b): Mean values of NT- pro BNP in correlation with LVEF

One way ANOVA was applied to calculate the mean Trop I which was 12.2±6.81 ng/ml, 9.5±8.63ng/ml and 3.0±5.41ng/ml for LVEF ≤40%, 41-49% and >50% respectively while NT-pro BNP was 7136.4±7.97pmol/l, 2328.9±3498.6pmol/l and 441±283.6pmol/l for LVEF ≤40%, 41-49% and >50% respectively. We found significant mean difference for Trop I (p=0.000) and NT- proBNP (p=0.000), Table 2.

Table 2: Mean comparison of Troponin I and NT-ProBNP according to LVEF dysfunction

LVEF		TROPONIN I		NT-Pro BNP	
		Mean Difference	p-value	Mean Difference	p-value
50% or >50%	41-49%	-6.47*	0.002	-1887.46	0.347
	≤40%	-9.16*	0	-6695.00*	0.000*
41-49%	50% or >50%	6.47*	0.002	1887.46	0.347
	≤40%	-2.69	0.106	-4807.53*	0.000*
≤40%	50% or >50%	9.16*	0	6695.00*	0.000*
	41-49%	2.69	0.106	4807.53*	0.000*

LVEF: left Ventricular ejection fraction
**Significant at 0.05 level*

Troponin I [AUC=0.706(0.620-0.791, p-value=0.000] and NT-pro BNP [AUC=0.870(0.813-0.926), p-value=0.000] had higher areas under curves, demonstrating the model's improved ability to differentiate between the positive and negative classes. Figure 2.

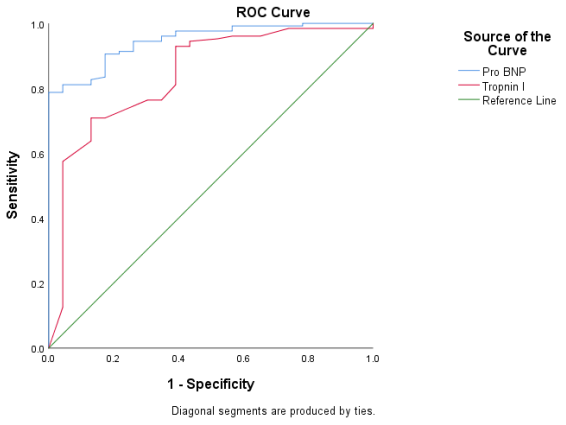

Figure 2: ROC curve comparing the sensitivity and specificity of Trop I and NT-proBNP for predicting LVEF by echocardiography.

DISCUSSION

The 76 amino acid residue amino (N)-terminal portion of pro-BNP which circulates normally in the human plasma has been reported to have elevated levels in case of cardiac dysfunction.[5,6] One of the things

suggesting that Pro-BNP is a more discerning marker is the fact that normally in humans its mean plasma concentration is similar to that of BNP that is approximately 10pmol/liter but in case of any cardiac impairment, the absolute and proportional increase above normal levels of NT-proBNP are more than those for BNP. After myocardial infarction (MI) it serves as an independent prognostic marker of mortality or decompensated heart failure.[7-9]

The secretion of NT-proBNP from the ventricles and its elevated levels following an acute myocardial infarction has been prominently associated with left ventricular systolic dysfunction. The development of heart failure and mortality after acute MI was thought to have an association with rising levels of NT-proBNP in the studies that have been conducted in the past. The left ventricular ejection fraction (LVEF) and 2 years of survival following an AMI has been predicted independently by using the values of cardiac biomarker NT-proBNP which was estimated approximately 2 to 4 days after the event.[10-12] There is a rapid rise in the levels of NT-proBNP over the first 24 hours after acute myocardial infarction which then tends to stabilize. After AMI the elevated levels of NT-proBNP was useful in identifying patients at risk for heart failure.

It has been observed that the elevated levels of NT-proBNP when quantified within a week of AMI help in the identification of patients that are at risk for heart failure, LV dysfunction and even death.[13,14] Regarded as one of the cardiovascular markers of both short- and long-term prognosis in patients who present in the setting of acute myocardial infarction it serves an important role for treatment and further management of these patients.[15,16] Studies in the past have shown that in patients presenting with Acute coronary syndrome the Pro BNP levels increased initially reaching a maximum level within forty-eight hours. It has also been documented that the release of BNP starts immediately after AMI event and takes 16 hours to reach peak.[17, 18]

When compared with patients having unstable angina those who suffered from the ST-elevation myocardial infarction patients were found to have significantly increased levels of Pro-BNP which could be because of a larger area of ischemia. The release of BNP and NT-pro BNP might be caused by myocardial ischemia which results in ventricular dysfunction that maybe temporary or permanent. The extent of ischemic injury is reflected by the magnitude of increase in the level of the marker soon after the onset of myocardial ischemia. NT-pro BNP was found superior when compared to TnI in terms of accuracy regarding prognosis. Along with several other risk factors which include age, renal impairment, history of previous heart failure and hypertension, elevated levels of NT-pro BNP and BNP also serve as a risk factor for adverse outcomes.[19,20] In our study although both biomarkers showed an inverse relationship with left ventricular systolic function, NT-Pro BNP showed superiority over Trop I in predicting the LVEF following an acute STEMI.

Limitations: This study was performed at a single center and the sample size was small

CONCLUSION

In patients presenting with first ST-elevation myocardial infarction undergoing primary PCI when the cardiac biomarkers were compared in terms of predicting the left ventricular ejection fraction, NT-proBNP was found to be superior to Troponin I.

AUTHORS' CONTRIBUTION

KUS and AF: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AS, SS, SA, and AZ: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

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Address for Correspondence:

Dr. Abeer Sarfaraz, Senior Registrar at Liaquat National Hospital, Karachi, Pakistan.
Email: abeer_sana@hotmail.com