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N-Terminal Pro Brain Natriuretic Peptide(NT – ProBNP) For Risk Stratification in Acute Coronary Syndrome (ACS)

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Abstract

Background: In detecting the whole spectrum of acute coronary syndromes (ACS) and for mortality prediction, natriuretic peptides (BNP and NT-proBNP) are useful tools for risk stratification of acute myocardial ischemia patients. **Aim:** This study assess the use of natriuretic peptides for early risk stratification of patients with acute coronary syndrome. **Results:** The p-value was >0.05N i.e. non-significant difference between the two groups for all the baseline characteristics of the studied population by NT-proBNP. The difference between the two groups for patients who had ST segment deviation was non-significant. T wave changes were significant between the two groups. In Group B (with NT-proBNP equal or more than 474 pg/ml), incidence of heart failure and duration of hospital stay were significantly higher when compared to Group A (with NT-proBNP less than 474 pg/ml),. In Group B, the number of coronary vessels affected, degree of stenosis and proximal left anterior descending artery (LAD) disease were higher when compared to Group A. In Group B compared to Group A, there was an increased incidence of cardiogenic shock and mortality.**Conclusion:** This study proved that NT-proBNP in acute coronary syndrome is an appropriate marker associated with more coronary artery involvements based on number of vessels affected and severity of stenosis. It is a valuable marker for higher heart failure incidence and lower ejection fraction.

Keywords: Acute coronary syndrome, Myocardial infarction, C-reactive protein..

Introduction

In choosing appropriate care and in determining prognosis of acute coronary syndrome (ACS), risk of stratification of patients with ST-elevation myocardial infarction(STEMI) or without persistant ST-elevation (NSTE-ACS) is primary[1].Since evidence based treatments such as anti-platelet, anti-thrombotic, revascularization techniques improves the cost-effectiveness of patient care, it can be a benefit from their use and be a target to the patients[2]. Clinical history, examination findings, changes of ECG, markers of damage of myocardium particularly cardiac troponin are the factors which affect risk assessment. In order to maximise the potential benefit of early risk assessment, the prognostic indicators should be made available at

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the time of initial evaluation of patient[3]. The cardiac troponin markers are inaccurate, despite careful integration of key variables of prognostic such as clinical, electrocardiographic, biochemical indicators, therefore there is need for new prognostic indicators[4]. Therefore, the ideal biomarker which possess many characteristics and which is emerging evidence is natriuretic peptides. Other advantage of these immunoassays are that they are available at reasonable cost. Three classes of natriuretic peptides are available. Chronic heart failure (CHF) functional status and diagnosis of heart failure have been aided by both BNP and NT-pro BNP[5]. Left ventricular dilatation, remodelling, and dysfunction as well as heart failure and death among patients with acute myocardial infarction are correlated to levels of BNP and NT-pro BNP. The strong association between levels of BNP and NT-pro BNP and mortality among patients without myocyte necrosis show that the BNP level will reflect extent or severity of insult of ischemia even when irreversible injury has not occurred. This study assess

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the use of natriuretic peptides for early risk stratification of patients with acute coronary syndrome.

Materials and Methods

This study was conducted in Osmania Medical College, Hyderabad during a period of January 2014 to February 2016. 130 patients presenting with acute coronary syndrome, 63 patients with unstable angina(UA), 45 patients with non-ST segment elevation myocardial infarction (NSTEMI) and 22 patients with ST segment elevation myocardial infarction (STEMI). A written consent was taken from all the patients and ethical committee approval was taken. A clinical examination, ECG, echocardiography, routine laboratory tests including serum creatinine, serial troponin I, creatine kinase, c-reactive protein and NT-proBNP at the time of admission was conducted for all patients. Within 48 hours of admission, coronary angiography,

percutaneous coronary intervention (PCI) were carried out. The patients were divided into two groups based on the levels of NT-proBNP. Group A had NT-proBNP less than 474 pg/ml and Group B had NT-proBNP ≥474 pg/ml. The comparison factors were risk factors, major adverse cardiac events, clinical characteristics, fraction of ejection, angiographic parameters including site, degree of stenosis which was assessed quantitatively, lesions numbers, number of vessels affected, LAD versus non-LAD lesions and proximal versus distal lesions. Microsoft excel was used for statistical analysis. Chi-square test was used to compare the categorical variables which were expressed as percentage. Students t-test was used to compare the continuous variables which were expressed as mean and standard deviation. If P value was <0.05, then the results were considered significant.

Results

Table 1: Baseline clinical characteristics of the studied population by NT-proBNP.

Clinical Characteristics	Group A (n=52)	Group B (n=78)	P value
Median Age (in years)	56.8 ± 8.9	58.57 ± 12.5	>0.05
Male gender (%)	40 (76.9%)	50 (64.1%)	>0.05
Obesity (%)	19 (36.5%)	28 (35.9%)	>0.05
BMI (mean ± SD)	29.6 ± 4.88	29.2 ± 6.9	>0.05
Diabetes (%)	35 (67.3%)	52 (66.6%)	>0.05
Hypertension (%)	38 (73.07%)	60 (76.9%)	>0.05
Smoking (%)	28 (53.8%)	32 (41.02%)	>0.05
Hyperlipidemia (%)	48 (92.3%)	66 (84.6%)	>0.05
Previous MI (%)	10 (19.2%)	30 (38.5%)	>0.05
Angina history (%)	24 (46.2%)	46 (59%)	>0.05
Previous PCI (%)	14 (27%)	18 (23.07%)	>0.05
History of CABG (%)	4 (7.7%)	6 (7.7%)	>0.05

MI- Myocardial infarction, PCI- percutaneous coronary intervention, CABG- coronary artery bypass graft.
The p-value was >0.05N i.e. non-significant difference between the two groups for all the baseline characteristics of the studied population by NT-proBNP.

Table 2: ECG, Laboratory and echocardiographic characteristics of the studied population.

Characteristics	Group A (n=52)	Group B (n=78)	P value
Patients who had ST segment deviation	19 (36.5%)	34 (43.6%)	>0.05
T wave changes (%)	19 (36.5%)	52 (66.6%)	<0.05
Ejection Fraction (%)	44.2 ± 6.5	35.8 ± 10.8	0.005
C-reactive protein (mg/dl)	16.2 ± 32.7	14.8 ± 30.9	0.69
Troponin pre angio	0.8 ± 2.7	6.1 ± 22.7	0.188
Troponin post angio	1.28 ± 2.2	7.7 ± 46.8	0.258

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Creatine kinase pre angio (ng/ml)	353.6 ± 825.8	222.8 ± 502.7	0.2
Creatine kinase post angio (ng/ml)	325 ± 489.11	301.5 ± 118.8	0.620
Serum Creatinine (mmol/L)	100.5 ± 66.6	120.8 ± 110.8	0.120
Glomerular Filtration rate	55.2 ± 9.8	52.68 ± 14	0.180

The difference between the two groups for patients who had ST segment deviation was non-significant. T wave changes were significant between the two groups.

Table 3: Angiographic characteristics of the studied population.

Characteristics	Group A (n=52)	Group B (n=78)	P value
Left anterior descending artery-LAD (%)	34 (65.4%)	64 (82.1%)	<0.05
Left circumflex artery-LCX(%)	18 (34.6%)	38 (48.7%)	>0.05
Right coronary artery-RCA (%)	20 (38.5%)	44 (56.4%)	>0.05
Single vessel disease (%)	12 (23.1%)	19 (24.4%)	>0.05
Double vessels disease (%)	21 (42%)	25(32.1%)	>0.05
Three vessels disease (%)	8(15.4%)	24(30.8%)	>0.05
Number of vessels (mean ± SD)	1.54 ± 1.01	1.89 ± 1.00	0.003
Degree of Stenosis (mean ± SD)	80 ± 24.1	88.8 ± 17.7	0.035
Proximal LAD lesions (%)	30 (57.7%)	50(64.1%)	0.001
Distal LAD lesions (%)	5 (9.62%)	4 (5.13%)	0.030
Thrombus (%)	7 (13.5%)	8(10.3%)	>0.05

Table 4: Prognostic characteristics of the studied population.

Characteristics	Group A (n=52)	Group B (n=78)	P value
Heart Failure	3(5.8%)	11(14.1%)	0.02
Cardiogenic shock	1(1.92%)	5(6.4%)	0.05
Mortality(%)	0(%)	3(3.84%)	0.05
Duration of hospital stay	4.0 ± 2.2	7.0 ± 3.3	0.004

Table 5: Comparison between different presentation of ACS regarding heart failure, EF and laboratory results.

Presentation of ACS	STEMI (n=22)	NSTEMI(n=45)	UA(n=63)
Ejection Fraction (%)	35.4 ± 7.7	36.4 ± 10.7	42.1 ±22.4
NT proBNP pre angio	2117±3115	1666±1477	1307±1748
NT proBNP post angio	3508.1±3287	2400.3±356	1498±2047
C-reactive protein	38.7±44.7	18.9±33.4	8.0±7.2
Troponin pre angio	7.99±14.8	7.96±25	0.18±0.14
Troponin post angio	30.7±88.7	1.0±1.1	0.12±0.34
CK pre angio	1111±1274	180.5±150.9	75.4±44.9
CK post angio	880.8±688	307.4±355	120.8±358

Discussion

In the present study, the p-value was >0.05N i.e. non-significant difference between the two groups for all the baseline characteristics of the studied population by NT-proBNP. The difference between the two groups for patients who had ST segment deviation was non-significant. T wave changes were significant between the two groups. In the study done by **Windhausen F et al**;[6]it was shown that several indicators of risk and severe coronary artery disease were associated with increased levels of NT-proBNP. Mortality by 1 year

was 7.3% in the highest quartile (> or = 1170 ng/L for men, > or = 2150 ng/L for women) compared with 1.1% of patients in the lower 3 quartiles (P < .0001). N-terminal pro-brain natriuretic peptide (highest quartile vs lower 3 quartiles) was a strong independent predictor of mortality (hazard ratio 5.0, 95% CI 2.1-11.6, P = .0002). However, the incidence of recurrent MI by 1 year was not associated with NT-proBNP levels. Hence, it could not be demonstrated that with an elevated NT-proBNP level, a benefit of an early invasive strategy compared with a selective invasive strategy in patients. **Renate Schnabel Hans J et al**[7] in their study, baseline samples from a prospective cohort of 904 consecutive patients with CAD. Cardiovascular events were registered during follow-up (median 2 years; maximum 3.7 years). Baseline Nt-proBNP was significantly higher among individuals with cardiovascular events compared with those without (711.5 vs. 238.8 pg/mL; **P**<0.0001). A similar association was found if the analysis was performed in patients who presented with stable angina (330 vs. 166.5 pg/mL; **P**=0.006) or acute coronary syndrome (990.9 vs. 527.7 pg/mL; **P**=0.03). In the SAP group, patients within the top quartile (>487.9 pg/mL) had a 3.7-fold (95% CI 1.2–9.1; **P**=0.01) increase in cardiovascular risk. After adjustment for most potential confounders including left ventricular ejection fraction, Nt-proBNP remained predictive for patients with serum concentrations in the upper quartile in comparison with patients in the lowest quartile (hazard ratio highest vs. lowest quartile: 4.0; **P**=0.03) (**n**=417).

Hanan Radwan et al[8]conducted a study in which there was a negative correlation between NT-proBNP and ejection fraction which was significant. In Group B (with NT-proBNP equal or more than 474 pg/ml) when compared to Group A (with NT-proBNP less than 474 pg/ml), incidence of heart failure and duration of hospital stay were significantly higher. In Group B compared to Group A, there was a trend to an increased incidence of cardiogenic shock and mortality. In Group B when compared to Group A, the number of coronary vessels affected, severity of stenosis and proximal left anterior descending artery (LAD) disease were higher. TIMI flow grade was significantly higher in Group A than in Group B. **Juan Sanchis et al**[9] showed that acute coronary syndrome was adjudicated to 79 patients (20%) and the composite endpoint to 59 (15%). The diagnosis of acute coronary

syndrome also increased (12%, 16%, 23% and 29%; P=.01),when the N-terminal pro-brain natriuretic peptide quartile increased, as did the risk of the composite endpoint (6%, 13%, 16% and 24%; P=.004). N-terminal pro-brain natriuretic peptide elevation (>125 ng/L) was associated with both endpoints (relative risk= 2.0; 95% confidence interval, 1.2-3.3; P=.02; relative risk=2.4; 95% confidence interval, 1.4-4.2; P=.004). However, in the multivariable models adjusted by clinical and electrocardiographic data, a predictive value was found for high-sensitivity T troponin but not for N-terminal pro-brain natriuretic peptide. **Marcello Galvani et al**[10]

Their results show that the prognostic value of natriuretic peptides is similar both at short- and long-term; when natriuretic peptides are measured at first patient contact or during hospital stay; for BNP or NT-proBNP; and in patients with ST elevation myocardial infarction or no ST elevation ACS.

These data suggest that natriuretic peptide measurement should be integrated into routine evaluation of patients with an ACS.

Conclusion

This study proved that NT-proBNP in acute coronary syndrome is an appropriate marker associated with more coronary artery involvements based on number of vessels affected and severity of stenosis. It is a valuable marker for higher heart failure incidence and lower ejection fraction.

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