Original Article

Assessment of Multiple Cardiac Biomarkers in Acute STEMI Patients without Clinical Manifestation of Heart Failure in NICVD

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Abstract

Background: *In patients with acute coronary syndrome (ACS), Cardiac Troponin I (cTnI) elevation is indicative of myocardial damage. After acute myocardial infarction (AMI), level of Pro-BNP rises rapidly during the first 24 hours and tends to stabilize thereafter.* ***Objective:*** *The present study tried to explore the pattern of multiple cardiac biomarkers (cTnI, CK-MB, Pro-BNP, SGOT and LDH) in newly diagnosed acute ST-elevation myocardial infarction (STEMI) patients without clinical symptoms of heart failure.* ***Materials and method:*** *This was a prospective study. Total 82 acute STEMI patients were recruited purposively from National Institute of Cardiovascular Disease (NICVD), Dhaka, Bangladesh, within 24 hours of symptoms having normal serum creatinine level. cTnI and pro-BNP elevation were defined >1mg/mL and >125 pg/mL respectively. The study population was sub grouped according to age: group A (<40 years), group B (40-50 years), group C (>51-60 years) and group D (>60 years).* ***Results:*** *The mean±SD age of patients was 53.3±11.6 years and 42.70% population belonged to relatively younger age group (group B). Smoking was found on the top of the list (73.20%) as a risk factor. There was no difference among the groups regarding atherosclerotic marker and no other cardiac markers except pro-BNP. Only Pro-BNP (pg/mL) showed gradual and progressive increment with increasing age. No significant difference was observed between CRP positive and negative groups in different age groups (cut off value <6mg/dL). Group B (40-50 years) seems to be the most vulnerable as the anterior and the extensive anterior myocardial infarctions (worst prognosis) were highest in this group.* ***Conclusion:*** *Worst prognosis is associated with increased age and raised pro-BNP level.*

Keywords: *Cardiac Troponin I; pro-BNP; STEMI; heart failure.*

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Introduction

Advances in our understanding of the pathophysiology of acute coronary syndrome (ACS) have led to the marked development of biomarkers for diagnosis, risk stratification,

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therapeutic decision-making, and assessment of clinical outcomes. Patients with ACS are subdivided into two major categories based on the 12-lead electrocardiogram (ECG); those with new ST-elevation on the ECG that is diagnosis of acute ST-elevation myocardial infarction (STEMI) and those who present with ST-segment depression, T-wave changes, or no ECG abnormalities [non ST elevation ACS (NSTEACS)].[1,2] Simultaneous evaluation of multiple cardiac biomarkers, which reflect different underlying pathophysiological processes, have been shown to offer complimentary prognostic information,[3-6] but professional guidelines have not advocated the routine use of a multimarker strategy because of the need for additional large studies of well-characterized patients with established risk indicators and the establishment of specific ties to therapy.[7-8] Although prior studies have utilized different combination of biomarkers, panels that include biomarkers representing the different underlying pathobiological processes in ACS have the greatest potential to provide incremental prognostic information. Evaluation of new biomarkers should also be conducted in the context of the two most established and studied biomarkers - troponin and natriuretic peptides.[9]

The third Global MI Task Force has continued the Joint ESC/ACCF/AHA/WHF efforts by integrating these insights and new data and recognizes that very small amounts of myocardial injury or necrosis can be detected by biochemical markers and/or imaging.[10] Several well designed studies have shown cardiac troponin (cTnI and cTnT) to be the most diagnostically sensitive and specific biomarker of myocardial injury.[11-13] B-type natriuretic peptide (BNP), an established biomarker for patients with heart failure, and its prohormone N-terminal pro BNP (NT-pro BNP) are elevated in patients with ACS and can identify ACS patients who are at higher risk for adverse cardiovascular events, including heart failure and death.[14-16]

Taking the advantage of availability of a large number of ACS patients in National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, the present study was done to explore the demography, atherosclerotic, cardiac and inflammatory markers in acute STEMI patients without clinical manifestation of heart failure. This study simultaneously tries to evaluate the incremental prognostic value of multiple biomarkers reflecting different underlying pathophysiological processes in a well-characterized population of patients with acute STEMI.

Materials and method

This study was conducted at the department of Biochemistry and Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, during the period of September to November, 2011. This was a prospective observational study. Total 82 acute STEMI patients admitted in CCU within 12 hours of onset of chest pain having normal serum creatinine level were purposively included. They had no clinical manifestation of heart failure within 24 hours of symptoms. Patients with unstable angina, non-STEMI, old MI, re-infarction, pregnancy and other congenital and vulvular heart diseases were excluded.

Patients admitted in CCU with the diagnosis of acute STEMI (type1 and type2)[10] after considering the inclusion and exclusion criteria were enrolled. Informed written consent was obtained from each study subject. Baseline data including demographic profile, clinical history and risk factors were recorded in a structured questionnaire on admission. Study population was divided into 4 groups according to age at the time of diagnosis - group A: < 40 years, group B: 40-50 years, group C: 51- 60 years and group D > 60 years.

Biochemical method

Blood samples (5 mL) were drawn and taken into heparin containing tubes: plasma prepared immediately by centrifugation by refrigerated centrifuge. cTnI and pro-BNP were measured by chemiluminescent immunometric assay (IMMULITE @ 1000, SIEMENS, USA). C-reactive protein (CRP) test was done by rapid latex slide agglutination method using CRP latex reagent, UK. Other parameters were tested by automation (CHEMWELL, AWARENESS, USA).

Statistical Analysis

All analyses were done using SPSS (Statistical Package for Social Science) for windows version 12. Values were expressed as mean(±SD) and percentage. One way ANOVA was applied to compare among groups. Chi square test was done for categorical data. Statistical significance was considered to be indicated by a p value of less than 0.05 in all cases.

Results

Table I shows that out of total 82 patients, 87.8% were male and rest (12.2%) were female. The mean±SD age of study population was 55.3±11.6 years. Among total patients 11 (13.40%) patients belonged to group A (< 40 years), 35 (42.70%) in group B (40- 50 years), 30 (36.60%) in group C (>51- 60 years) and 6 (7.30%) in group D (> 60 years). The mean±SD BMI was 23±2.6 and 20.30% patients were overweight.

Table I: Demographic profile (N=82)

Variables	Variables
Sex	
Male	72 (87.8%)
Female	10 (12.2%)
Age (years)	
Mean±SD	55.3±11.6
Group A: < 40	11 (13.4%)
Group B: 40-50	35 (42.7%)
Group C: 51-60	30 (36.6%)
Group D: >60	6 (7.3%)
BMI (kg/m2)	
Mean±SD	23±2.6
>30 (Obese)	1.7%
18.5 – 24.9 (Normal)	78%
25 – 29.9 (Overweight)	20.3%

Table II shows the distribution of risk factors among study population. Smoking was found on top of the list in all groups (73.20%). Among other risk factors hypertension, (41.30%), diabetes mellitus (31.70%), positive family history (22%) and dyslipidaemia (14.60%) were found.

Table II: Risk factors in the study group (Multiple responses)

Risk factors	Groups (Frequency)				Total
	A	B	C	D	
Smoking	9	24	23	4	60 (73.13%)
Hypertension	3	11	16	4	34 (41.46%)
Diabetes Mellitus	2	11	12	1	26 (31.7%)
Positive family history	5	6	7	0	18 (21.95%)
Dyslipidaemia	2	5	5	0	12 (14.63%)

Table III reveals that all the groups were BMI matched. There were no significant differences regarding atherosclerotic marker [fasting blood sugar (FBS), total cholesterol (TC), triacylglycerol (TG), LDL-C and HDL-C] among the groups.

Table III: Distribution and comparison of atherosclerotic markers among groups (N=82)

Atherosclerotic Markers	Group (Mean±SD)				p value
	A (n = 11)	B (n = 35)	C (n= 30)	D (n=6)	
BMI (Kg/m^2)	24.0±12.3	23±2.2	23.2±3.1	20.4±2.4	0.10
FBS (mmol/L)	7.08±5.0	8.36±5.7	9.3±6.2	7.5±3.2	0.78
TC (mg/dL)	177±133.4	187.7±39.4	174.4±37.8	157.2±19.2	0.22
TG (mg/dL)	122.2±32.0	150.9±64	148.6±65	155.8±33.6	0.53
HDL-C (mg/dL)	51.8±34	39.9±24	42.6±17.2	35.2±3.8	0.40
LDL-C (mg/dL)	100.8±42.3	116.3±33.9	105.63±35	94.0±27.9	0.33

Table IV shows the distribution of cardiac biomarkers in groups. Among the cardiac markers only Pro-BNP (pg/mL) shows gradual and progressive increment with increasing age.

Table IV: Cardiac biomarker in study groups

Risk factors	Groups (Frequency)				Total
	A	B	C	D	
Smoking	9	24	23	4	60 (73.13%)
Hypertension	3	11	16	4	34 (41.46%)
Diabetes Mellitus	2	11	12	1	26 (31.7%)
Positive family history	5	6	7	0	18 (21.95%)
Dyslipidaemia	2	5	5	0	12 (14.63%)

Taking cut off value of 6 mg/dL for CRP, subjects were divided in to two groups. No significant difference was observed between CRP positive and negative groups in different age groups (Table V).

Table V: Comparison of CRP in different age groups (CRP < 6 mg/dL considered as negative) (N=82)

CRP	Group (Frequency)				p value
	A (n = 11)	B (n = 35)	C (n= 30)	D (n=6)	
Negative	4(36.36%)	17(48.57%)	17(56.67%)	3(50%)	0.71
Positive	7(63.64%)	18(51.43%)	13(43.33%)	3(50%)	

Table VI shows the distribution of pro-BNP level in CRP positive and negative group.

Table VI: Distribution of Pro-BNP in CRP positive and negative group (N=82)

CRP	Pro BNP(pg/mL)
Negative	2305.51±5757.45
Positive	5440.20±8418.52

Table VII shows that anterior (26.80%) and extensive anterior (26.80) MI was more in study group diagnosed by ECG.

Table VII: Area of infarcted myocardium by ECG in study group (Multiple responses)

ECG findings	Group (Mean±SD)				p value
	A	B	C	D	
Anteroseptal	1	8	4	1	14 (17.07%)
Lateral	1	0	3	0	4 (4.87%)
Anterior	3	15	7	1	26 (31.70%)
Extensive anterior	2	13	8	1	24 (29.26%)
Inferior	2	2	7	3	14 (17.07%)
Inferolateral	0	1	0	0	1(1.22%)

Table VIII reveals that out of total 82 patients 37.80% developed heart failure, 32.93% experienced post MI angina, 40.24% had significant arrhythmias, 30.49% went to cardiogenic shock and death occurred in 17.07% patients.

Table VIII: Outcome profile of study population (Multiple responses)

Out comes	Group (Mean±SD)				p value
	A	B	C	D	
Heart failure	1	15	13	2	31 (37.80%)
Post MI angina	0	16	11	0	27 (32.93%)
Significant arrhythmias	2	14	16	1	33 (40.24%)
Cardiogenic shock	1	13	10	1	25 (30.49%)
Death	0	9	2	3	14 (17.07%)

Discussion

The development of novel biomarkers in cardiovascular disease requires rigorous evaluation in the context of established tools. This analysis revealed the mean ages of patients were around 55 years and majorities were male. Another large study done earlier on Bangladeshi population revealed similar demographic profile of cardiac patients.[17] This is in agreement with the findings in several early studies[18-21], and trials[22] in USA. The recent COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) Trial[22] in USA shows the mean age of AMI patients is 62±5 years. Another recent study compared the ACS between South Asians and Caucasians. It showed that Asians were at least 10 years younger to the Caucasians at the time of presentation of ACS.[23] In Pakistan there is an observation from a study that up to 28% of the patients belong to the age group of 40-45 years.[24] In this study population, 78% of the patients had normal BMI (<25 kg/m^2), 20.30% were overweight (BMI>25-29.9 kg/m^2) and 1.7% were obese (BMI>30 kg/m^2). A study in Europe showed 29.60% patients were of normal weight, 46.80% were overweight and 24.40% obese.[25]

In risk factors analysis smoking was found at the top of the list (73.20%) followed by history of hypertension 41.30% and diabetes 31.70%. An earlier study in NICVD, showed that 54.60% patients had history of smoking and all of them were male, diabetes mellitus was present in 38.90% patients and 20.40% patients had hypertension.[26] Another study in NICVD showed 80% patients had history of smoking; history of hypertension was present in 46% patients and diabetes mellitus was present in 34% patients.[27]

There were no significant difference of level of concentration of cTnI, CK-MB, SGOT and LDH among groups except pro-BNP. Pro-BNP was significantly higher in > 60 years age group.

There was no significant difference of CRP level in different age group but concentration of pro-BNP level was significantly higher in CRP +ve group. A large population based study concluded that combination of NT-pro BNP with creatinine clearance rate, heart rate, or levels of troponin T or CRP provides a better risk stratification concerning mortality in ACS patients.[28]

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