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EC CARDIOLOGY
Research Article

Raised Level of Cardiac Troponin I (50 Folds Upper Limit of Normal) is a Sensitive and Specific Marker for Extent of Coronary Artery Disease in First Attack of Non-ST Segment Elevation Myocardial Infarction in Bangladeshi Population

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Received: February 21, 2019; **Published:** July 18, 2019

Abstract

Background: Coronary heart disease (CHD) is the single most important cause of death. Diagnosing ACS is important because the diagnosis triggers both triage and management. Cardiac Troponin-I (cTnI) known to be a very sensitive and specific marker for extent of coronary artery involvement.

Objective of the Study: The study aimed to determine the correlation of extent of coronary artery disease (CAD) with elevation of Troponin - I level in Non-ST-elevation myocardial infarction (NSTEMI).

Methods: This cross-sectional analytical study was conducted from middle of 2016 to that of 2017. Total 230 first attack of NSTEMI patients were included in the study. All patients underwent coronary angiography in different tertiary care hospital where coronary angiography facility is available. Single, double or triple vessel CAD were considered for extent of CAD. The sample population was divided into two groups: Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml. Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml. Association between cTnI levels and CAD extent were observed statistically**.**

Results: Out of 230 patients, in 111 patients of Group-I, majority (36%) had double, then 30.6% had triple vessel and the remaining had single vessel CAD, whereas in 119 patients of Group - II, most patients (46.2%) had triple vessel, then 31.1% had double and the rest had single vessel CAD. The results indicated statistically significant association between the cTnI levels and triple vessel CAD ($p = 0.04$). Our study discovered that increased Troponin-I level over 6.6 ng/ml is a very sensi**tive and specific for CAD extension.**

Conclusion: The study enabled us to conclude that, higher cTnI levels are associated with an increased extension of CAD involvement.

Keywords: *Troponin-I; NSTEMI; Coronary Artery Disease (CAD); Sensitivity; Specificity*

Introduction

Among patients presenting with acute coronary syndrome (ACS), multiple segments of the coronary arterial tree exhibit plaque disruption or frank rupture, which is possibly related to a pan-inflammatory process [1], hence it is uncommon to see non-obstructive coronary artery disease (CAD) or a normal coronary angiogram in patients undergoing coronary angiography for ACS [2]. Prognoses in patients with ACS are related to the level of cardiac biomarker release [3]. It has been demonstrated that this subset of patients has extensive CAD compared to patients with undetectable troponins [4,5]. It is essential to further investigate whether the degree of increase

in troponin levels in the setting of NSTEMI equates with severe multi-vessel CAD. In our investigation cardiac Troponin - I (cTnI) has been found to have excellent sensitivity and specificity and is superior to others as indicator of extent of coronary artery disease.

Materials and Methods

This prospective analytical study was conducted from middle of 2016 to that of 2017. Study population comprised all the patients admitted into Cardiology department with chest pain. Sample population were selected by brief history, targeted physical examination, ECG, Troponin-I level (> 0.12 ng/ml) on admission and after 06 hours if the initial value was negative and on the basis of inclusion and exclusion criteria. The ethical review committee endorsed the study protocol.

Inclusion criteria

- Patients with first attack of NSTEMI.

Exclusion criteria

- Patients admitted with acute STEMI.
- Patients with valvular heart disease, congenital heart disease and cardiomyopathy.
- Patients had major non- cardiovascular disorder causing elevation of Troponin-I.
- Any systemic infection.
- Patients were under chemotherapy on discovery of malignancy.
- Patient not willing to get themselves enrolled in study.

Considering inclusion and exclusion criteria study population was divided into two groups:

1. **Group-I:** Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.
2. **Group-II:** Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

NSTEMI was defined as positive biomarkers of myocardial necrosis (troponin-I) with or without ST-segment depression in the absence of ST-segment elevation. Blood samples for cardiac troponin I were drawn in emergency and a second sample was drawn 06 hours later if the initial sample was negative. Cardiac troponin I was determined using an immunometric assay (IMA) technology. All recruited patients underwent invasive evaluation by coronary angiography in facilitated tertiary hospitals. Angiographic views were analyzed for extension of coronary artery disease. Significant CAD was defined as ≥ 70% stenosis in the major epicardial coronary arteries or a left main coronary artery stenosis ≥ 50%. Extent of CAD was defined as significant single, double or triple vessel CAD involvement.

Statistical method and analysis

Purposive sampling was done. The collected data were analyzed with the aid of computer software Statistical Package for Social Sciences version 20 (SPSS Inc., Chicago, Illinois). Quantitative data were expressed as mean ± SD and Student's "t" test was employed for analysis. Qualitative data were analyzed with χ^2 test. Comparison between groups were made by unpaired t-test. p value < 0.05 was taken as significant.

Variables studied

Age, Sex, Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, F/H of CAD, BMI, ECG, Troponin-I, Extent of CAD.

Results

This was a Cross Sectional Analytical Study conducted in the Cardiology department of Mymensingh Medical College Hospital from middle of 2016 to that of 2017. The research team tried to ascertain elevated level of Troponin-I as a sensitive and specific marker for extent of coronary artery disease in the setting of first attack of NSTEMI.

Variable	cTnI ≤6.6 ng/ml (n = 111)	cTnI ≥6.6 ng/ml (n=119)	p value
Age	59.40 ± 9.81	59.30 ± 12.18	
30 - 44	03 (2.8%)	16 (13.4%)	
45 - 59	54 (48.6%)	40 (33.6%)	
60 - 74	50 (45.0%)	56 (47.1%)	
75 - 89	04 (3.6%)	07 (5.9%)	
Gender			
Male	82 (73.9%)	87 (73.1%)	0.621^{ns}
Female	29 (26.1%)	32 (26.9%)	
BMI	25.07 ± 3.55	24.65 ± 4.21	0.417^{ns}
Troponin-I level (ng/ml)	5.53 ±7.43	16.46±15.79	0.003^{s}
Cardiac Risk Factors			
Diabetes mellitus	55 (49.5%)	60 (50.4%)	0.595^{ns}
Hypertension	76 (68.4%)	84 (70.5%)	0.235^{ns}
Cigarette smoking	27 (24.3%)	37 (31.0%)	0.784^{ns}
Positive F/H of CAD	25 (22.5%)	26 (21.8%)	0.690^{ns}
Dyslipidaemia	78 (70.2%)	69 (57.9%)	0.294^{ns}
	74 (66.6%)	75 (63.0%)	0.235^{ns}

Table 1: *Baseline characteristics of patients according to the cardiac troponin I level status (n = 230).*

cTnI means Cardiac Troponin-I. ns means not-significant. F/H means Family History.

CAD means Coronary Artery Disease. ECG ischaemic abnormality i.e. ST segment depression (> 0.5 mm) or prominent T wave inversion.

Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.

Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

There were 73.4% males and 26.5% females with the mean age of 59.35 ± 11.08. Among them 50% were diabetic, 69.5% were hypertensive and 63.9% were dyslipidaemic. There were 27.8% smokers and 22.2% patients had positive family H/O CAD. Mean cardiac troponin I level was 5.53 ± 7.43 in the cTnI ≤ 6.6 ng/ml group and mean 16.46 ± 15.79 in the cTnI > 6.6 ng/ml group. Patients with less troponin I level tend to be more dyslipidaemic 70.2% versus 57.9%, while patients with elevated troponin I level had a higher incidence of smoking 31.1% versus 24.3%, a higher proportion of patients age less than 45 years, 84.2% versus 15.8% and also of age greater than 75 years, 63.6% versus 36.4%.

	cTnI ≤6.6 ng/ml (n=111)		cTnI ≥6.6 ng/ml (n=119)		p value
Extent of CAD					0.13^{ns}
Single vessel CAD	25	(22.5%)	23	(19.3%)	0.35^{ns}
Double vessel CAD	40	(36.0%)	37	(31.0%)	0.21^{ns}
Triple vessel CAD	34	(30.6%)	55	(46.2%)	0.04^{s}
Left Main Stenosis (> 50%)	6	(5.4%)	12	(10.0%)	0.761^{ns}
Branch Vessel CAD	7	(6.3%)	3	(2.5%)	0.56^{ns}
Non-obstructive CAD	2	(1.8%)	0 (0%)		0.21^{ns}
Normal Coronary Angiogram	3	(2.7%)	1	(0.8%)	0.34^{ns}
Total occlusions					0.14^{ns}
Single vessel	27	(24.3%)	40	(33.6%)	0.12^{ns}
Double vessel	15	(13.5%)	23	(19.3%)	0.23^{ns}
Triple vessel	5	(4.5%)	5	(4.2%)	0.91^{ns}

Table 2: *Extent of coronary artery disease and number of totally occluded vessels in the study population (n=230).*

cTnI means Cardiac Troponin-I. ns means not-significant. s means Significant.

CAD means Coronary Artery Disease.

Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.

Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

Table 2 compares the extent of CAD and the number of occluded vessels among the two groups of cardiac troponin I. At coronary angiography, among the 111 patients with cTnI levels ≤ 6.6 ng/ml, the rates of significant single, double and triple vessel CAD were 22.5%, 36% and 30.6% respectively. While among the 119 patients with cTnI levels ≥ 6.6 ng/ml, the rates were 19.3%, 31.1% and 46.2% respectively (p = 0.35, p = 0.21 and p < 0.04 respectively) which was not statistically significant (p = 0.13). Furthermore, in patients with cTnI ≥ 6.6 ng/ml, there were also a greater proportion of patients with left main coronary artery stenosis (> 50% stenosis) and a greater number of totally occluded vessels.

Site of coronary lesion	cTnI ≤ 6.6 ng/ml (n = 111)		cTnI ≥ 6.6 ng/ml (n = 119)	
LMCA	6	(5.4%)	12	(10.0%)
LAD	97	(87.3%)	104 (87.3%)	
Proximal	42	(37.8%)	50	(42.0%)
Mid-distal	55	(49.5%)	54	(45.3%)
Diagonal	23	(20.7%)	37	(31.0%)
LCX	46	(41.4%)	74	(62.1%)
Proximal	24	(21.6%)	40	(33.6%)
Mid-distal	22	(19.8%)	34	(28.5%)
Obtuse Marginal	34	(30.6%)	33	(27.7%)
LPLB	6 (5.40%)		10 (8.4%)	
LPDA		0	4	(3.3%)
RCA	79	(71.1%)	82	(68.9%)
Proximal	28	(25.2%)	29	(24.3%)
Mid-distal	51	(45.9%)	53	(44.5%)
RPLB	6	(5.4%)	5	(4.2%)
RPDA	8	(7.2%)	8	(6.7%)
RI	3	(2.7%)	9	(7.5%)

Table 3: *Relation between cardiac troponin I levels and the site of coronary lesion (n : 230).*

cTnI: Cardiac Troponin I; LMCA: Left Main Coronary Artery; LAD: Left Anterior Descending Artery; LCX: Left Circumflex Artery; LPLB: Left Postero-Lateral Branch; LPDA: Left Posterior Descending Artery; RCA: Right Coronary Artery; RPLB: Right Postero-Lateral Branch; RPDA: Right Posterior Descending Artery; RI: Ramus Intermedius Artery. Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.

Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

Table 3 summarizes the angiographic characteristics of patients in the two cutoff levels of cTnI with respect to the site of significance (>70%) coronary stenosis. The left anterior descending artery (LAD) was the vessel most commonly involved with significant stenosis in both the groups. In patients with cTnI levels ≤ 50 folds ULN, LAD was the commonest vessel 97 (87.3%), followed by right coronary artery (RCA) 79 (71.1%) and then left circumflex artery (LCX), 46 (41.4%). While in patients with cTnI levels >50 folds ULN, LAD was the commonest vessel, 104 (87.3%), followed by RCA 82 (68.9%) and then LCX artery 74 (62.1%). In patients with cTnI levels > 50 folds ULN, there was also more involvement of the diagonal branch, left posterior descending artery and left postero-lateral branches.

	Extent of CAD		p-value
Troponin-I (ng/ml)	Group-I (n = 111)	Group-II (n = 119)	
≥ 6.6	03	108	< 0.00001[s]
< 6.6	108	11	

Table 4: *Comparison of Troponin-I level and Left Ventricular Ejection Fraction (LVEF) between the groups (n = 230).Chi-Squire test was done.*

Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.

Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

The above table shows majority of the study subjects of group-I had troponin-I level ≤ 6.6 ng/ml and majority of the study subjects of group-II had troponin-I level ≥ 6.6 ng/ml. Here, the difference between the two groups was statistically significant (P < 0.05).

Parameter		p-value
Age	0.20	0.57^{ns}
Sex	-0.06	0.723^{ns}
BMI	0.10	0.12^{ns}
Smoking	0.142	0.813^{ns}
HTN	-0.194	0.325^{ns}
DM	0.233	0.435^{ns}
F/H of CAD	-0.005	0.565^{ns}
Dyslipidaemia	-0.229	0.113^{ns}
Extent of CAD	-0.182	0.001^{s}
ECG	0.004	0.324^{ns}
Troponin-I	0.261	0.002^{s}

Table 5: *Multivariate regression analysis of the risk factors of the study population (n = 230).*

Multivariate linear regression analysis was done. s means significant. ns means not- significant.

The multivariate regression analysis was done for the variables studied which showed regression co-efficient for Troponin-I and Extent of CAD were statistically significant (p < 0.05) but the other parameters revealed no statistical significance.

	Extent of CAD	
Troponin-I (ng/ml)	**Group-I (n = 111)**	**Group-II (n = 119)**
≥6.6	03 (b)	108 (a)
<6.6	108 (d)	11(c)
Sensitivity		91%
Specificity		97%

Table 6: *Sensitivity and Specificity of Troponin-I level for Extent of CAD (n = 230).*

a = true positive c = false negative. b = false positive d = true negative.

Group-I: Patients with first attack of NSTEMI with Troponin-I level ≤ 6.6 ng/ml.

Group-II: Patients with first attack of NSTEMI with Troponin-I level ≥ 6.6 ng/ml.

The above table shows the sensitivity and specificity of Troponin-I level for left ventricular systolic dysfunction were 91% and 97% respectively.

Discussion

The present study provides insight into the association between the two cutoff levels of cardiac troponin I (≤ 50 folds ULN and > 50 folds ULN) in NSTEMI and the number of major epicardial coronary vessels that have significant luminal narrowing (> 70% stenosis). The study demonstrated that among patients with cTnI levels ≤ 6.6 ng/ml, 22.5% of the patients had single vessel, 36% had double vessel and 30.6% had triple vessel significant for CAD, while among patients with cTnI levels ≥ 6.6 ng/ml, 19.3% of the patients had single vessel, 31.1% had double vessel and 46.2% had triple vessel significant CAD. We found a statistically significant relationship only

between cTnI level ≥ 6.6 ng/ml and triple vessel CAD. Due to absence of local data for such an association we took the challenge for such a research. Our study revealed that 2.7% patients with cTnI ≤ 6.6 ng/ml and only 0.84% patient in the cTnI ≥ 6.6 ng/ml group had a normal coronary angiogram. In patients with NSTEMI, there are more extensive disease when troponin levels are elevated [6,7]. A study analyzed clinical and angiographic variables and found patients with troponin I levels (≤ 10 folds ULN), frequently had higher Braunwald Class angina [4], more severe ECG changes, higher proportion of extensive CAD. cTnI concentration ≥ 6.6 ng/ml predicted multi-vessel coronary artery disease with a sensitivity of 100% and specificity of 92.4% respectively [9]. In our study, we found that Troponin-I level ≥ 6.6 ng/ml has got 91% patients with multi-vessel coronary artery disease. On the other hand, Troponin-I level ≤ 6.6 ng/ml has got 9% patients with multi-vessel coronary artery disease. The difference is statistically significant between two groups ($p < 0.05$). Our study also discovered that Troponin-I level ≥ 6.6 ng/ml is predictive of multi-vessel coronary artery disease with a sensitivity and specificity of 91% and 97% respectively which is quite similar to other studies [9,10]. Overall, the results of our study suggest that elevated troponin I levels are associated with a greater severity and extent of coronary artery disease in the setting of NSTEMI. We hypothesised that levels of Troponin-I could be correlated with extent of coronary artery disease following NSTEMI. From the above discussion we found that in patients with first attack of NSTEMI, Troponin-I level serves as a very sensitive and specific marker for extent of coronary artery disease.

Limitations of the Study

Several limitations of our study must be acknowledged:

- The severity and location of the coronary lesions was based on the operator visual estimation.
- The majority of the study population were male. Thus, these results need to be re-evaluated in other health care center by incorporating male and female in large numbers.
- The study evaluated the extent of CAD in terms of the number of severely diseased major coronary arteries with respect to the two cutoff levels of cTnI.
- Troponin-I level estimation have become more easier and more sensitive by using the newer methods. Due to infrastructural limitations our patients' blood sample was analyzed with the aid of traditional technique.

Conclusion

The present study concluded that the higher the Troponin-I level surrogates for higher sensitivity and specificity for extent of coronary artery disease.

Recommendation

Based on the findings of the study, we have been able to suggest the following measures to ensure a more scientific diagnosis, prognosis and treatment of the patients afflicted with Non- ST segment elevation myocardial infarction.

In perspective of our country, Troponin-I is an available test for making diagnosis and to see prognosis in acute MI patients. Troponin-I level have an impact over left ventricular ejection fraction in patients with Non-ST segment elevation myocardial infarction. Troponin-I level provides a note warning about the outcomes of the patients after NSTEMI. A number of studies were conducted in past for acute MI patients, mostly on ST- segment elevation myocardial infarction. Few studies were conducted regarding Non-ST segment elevation myocardial infarction. As, extent of coronary artery disease was correlated well with troponin-I levels; So, Troponin-I alone can serve dual purpose - for both diagnosis and prognosis of NSTEMI Patients.

The study also recommends that aggressive treatment strategy including early PCI and closer surveillance should be offered to NSTEMI patients with high Troponin-I levels, as these patients are more prone to develop complications like heart failure, arrhythmia and even sudden cardiac death.

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Volume 6 Issue 8 August 2019