ORIGINAL RESEARCH PAPER

Biochemistry

COMPARATIVE EVALUATION OF DIAGNOSTIC MARKERS IN MYOCARDIAL INFARCTION

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Background: Myocardial Infarction is the process of myocardial cell death due to ischemia or Imbalance between the supply and demand of oxygen within the coronary arteries. The study of cardiac markers like Troponin T, Troponin I, CK-MB and NT-Pro BNP are being used currently in the assessment of Myocardial Infarction.

Methods: The study was conducted at cardiac center of Mahavir cardiac hospital , Surat. A total of 222 patients of suspected myocardial infarction presented within 12hrs of onset of symptoms were enrolled. They were diagnosed for MI using various Biochemical Markers like Troponin T, Troponin I, CK-MB, NT-Pro BNP and other radiology test like ECG, Echo and Angiography. The confirmation of event of MI was done by the respective physician by checking all the test result as well as clinical checkups.

Result: We found 88.5% sensitivity and 64.7% specificity for Troponin T as compare to Troponin I(85.7% and 45.5%) , CPK-MB (64.3% and 37.5%) and NT-Pro BNP (66.7% and 54.7%).

Conclusion: Troponin T offers higher sensitivity and specificity as compare to other markers for diagnosis of Myocardial Infarction and valuable tool for risk stratification in patient with acute chest pain.

INTRODUCTION

Myocardial infarction (MI) defined by the presence of 2 of the 3 following characteristics.[1]

I.   Symptoms of acute ischemia(chest pain)
II. ECG changes (ST segment elevation or depression)
III. Increase of enzymes in the blood (combination of total creatine kinase (CK), CK-myocardial band (MB), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH).

Acute Myocardial Infarction is one of the major disease or disorder that leads to death with ongoing incidence globally [2]. Myocardial infarction(MI) is the process of myocardial cell death due to ischemia or the imbalance between supply and demand within the coronary arteries as a consequences of thrombotic process[3]. Early diagnosis and control of Myocardial infarction is important with frequency of ischemic heart disease, at that time cardiac biomarkers are essential [4]. The electrocardiogram (ECG) is often indistinct in the early hours of an incident, and even in the case of infarction in patient with acute chest pain[5]. Variable spectrum of symptoms have been observed in acute MI, in some of the cases only ECG results are not enough for correct diagnosis, which leads to diagnostic error, at that time cardiac enzymes and biochemical markers play the key role in diagnosis and detection of MI [4]. In early decisive phase the first option is ECG, which even if normal does not diagnose MI, then other biomarkers can use like CK-MB, Troponin T, Troponin I, SGOT, LDH and myoglobin[6]. Biomarker is defined as " a characteristic that is objectively measured and evaluated as an indicator of normal biological process or pharmacological response to a therapeutic intervention[7].

Troponin T (TnT) is a part of the troponin complex in striated muscles located on the thin filament of the skeletal and cardiac muscle fibers. Troponin C is not really specific for cardiac injury because isoform of troponin C is similar in the skeletal and cardiac muscle whereas Troponin T and I are truly specific for myocardial infarction as their isoform are differs in skeletal and cardiac muscle[8]. Cardiac Troponin T (cTnT) and troponin I (cTnI) are cardiac regulatory proteins that mediate interconnection of calcium between actin and myosin[9]. Creatine kinase-myocardial band (CK-MB) is an enzyme present primarily in cardiac muscle, increased with AMI[10]. It is useful because of shorter time to elevate but it is not preferred because of non-specificity[11]. N-terminal pro-brain natriuretic peptide (NT-Pro BNP) is a prohormone with a 76 amino acid N-terminal inactive protein cleaved from the molecule to release Brain natriuretic peptide[12]. BNP and NT-Pro BNP are produced due to ventricular stretch and myocardial injury[13]. The peptide is responsible for the maintenance of circulatory homeostasis and prevent the cardiovascular system from volume overload[14].

ST-elevation myocardial infarction (STEMI) is a clinical condition in which myocardial infarction is present with persistent electrocardiographic ST elevation (STE) and following release of biomarkers[15]. ST segment elevation myocardial infarction is an acute myocardial infarction which occurs due to rupture of cleavage of atherosclerotic plaque which leads to blockage of coronary artery.[16]

METHOD

The study was conducted at cardiac center of the Mahavir cardiac hospital, surat. A total of 222 patients of suspected myocardial infarction presented within 12hrs of onset of symptoms were enrolled. They were diagnosed for MI using various Biochemical Markers like Troponin T, Troponin I, CK-MB, NT-Pro BNP and other radiology test like ECG, Echo and Angiography. The confirmation of event of MI was done by the respective physician by checking all the test result as well as clinical checkups.

Present study includes the analysis of various biochemical markers. For the same blood was collected and serum was separated and freshly used for various analytical methods.

Quantitative determination of cardiac troponin T was done by electrochemiluminescence immunoassay "ECLIA" on Elecsys and cobas e immunoassay analyzers. Quantitative cardiac troponin I and NT-Pro BNP were done on the instrument of VIDAS, using ELFA technique [enzyme linked fluorescent assay]. The assay principle combines one step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The VITROS CKMB slide method was performed using the VITROS CKMB slides and the VITROS chemistry products.

RESULTS

Table 1: Level of Troponin T in confirmed MI (n=78) and non-MI patient (n=77)

	High Troponin T*	Normal Troponin T
Confirmed MI patient	88.5%	11.5%
Patient without MI	35.1%	64.9%

*more than 0.014 ng/ml is considered increased Troponin T level as suggested by the kit literature

Table 2: Level of Troponin I in confirmed MI (n=7) and non-MI patient (n=11)

	High Troponin I*	Normal Troponin I
Confirmed MI patient	85.7%	14.3%
Patient without MI	54.5%	45.5%

*more than 19 ng/L is considered High Troponin I level as suggested by the kit literature

In the present study, the sensitivity and specificity of Troponin T test were found to be higher than Troponin I, CPK-MB and NT- Pro BNP in the diagnosis of acute myocardial infarction. (Table 3)

Table 3: Sensitivity and Specificity of various parameter in diagnosis of myocardial infarction

	Troponin T	Troponin I	CPK-MB	NT-Pro BNP
Sensitivity (Tps × 100% / [TPs + FNs])	88.5%	85.7%	64.3%	66.7%
Specificity (TNs × 100% / [FPs + TNs])	64.7%	45.5%	37.5%	54.7%

(TPs: True Positives, FNs: False Negatives, TNs: True negatives, FPs: False Positives)

Table 4: Positivity of Troponin T (n=96) in relation to time from the onset of Myocardial Infarction.

Time	Troponin T
0-2hr	42.8%
2-4hr	60%
4-6hr	63.6%
6-8hr	84.2%
8-10hr	75%
10-12hr	72.7%

Table 5: Distribution of Chest Pain Patient Exhibiting ST Elevation and without ST Elevation (n=154) during initial period [up to 8hr]

No of patient	ST elevated	Non ST elevated
154	30.5%	69.5%

Table 6: Level of various parameters in confirmed MI patient

Troponin T(n=78)		Troponin I(n=7)		ST/non-ST segment elevation(n=63)	
Normal	High	Normal	High	ST elevation	Non-ST elevation
11.5%	88.5%	14.3%	85.7%	46.1%	53.9%

DISCUSSION

In this study sensitivity (88.5%) and specificity (64.7%) of Troponin T test was higher in comparison with the other enzymes like CPK-MB and NT-Pro BNP (table 3). In the study carried out by Sharma D. et al. 86 MI patient were considered for the study and in these sensitivity and specificity of Troponin T were 67.3% and 73.8% respectively which is higher than sensitivity (56.2%) and specificity (45.7%) of CK-MB[17]. In the study carried out by Baheti R. a total of 156 patient suspected of MI were considered for the study in which Troponin T test was done by card consisting of strip labeled by monoclonal antibodies for Troponin T and in these sensitivity and specificity were 64.7% and 71.4% respectively[18]. Even the higher sensitivity and specificity of Troponin T test of 95.2% and 93.8% were reported by Guo x et al[19].

In this study the sensitivity of Troponin T test was 84.2% and 75% after 8-10 hr of myocardial infarction but before 10hr it ranges from 42-63%. (Table 4). Thus, Troponin T has been found to be the most reliable marker while the period of 8-10hrs after onset of the symptoms. In the study carried out by Sharma D et al. found peak positivity of Troponin T after 10-12 hr [17]. In the study carried out by Ziemmerman. J et al. In 955 patients 13.7% ST segment elevation and In 119 patient with acute Myocardial Infarction 45.4% ST-segment elevation was observed. [20]

CONCLUSION

Cardiac markers have been implicated in the diagnosis and risk stratification, selection of therapy, monitoring disease progression and treatment efficacy. This study concludes, cardiac Troponin T is a sensitive marker for Diagnosis of myocardial Infarction, and plays the vital role for establishing the diagnosis of MI in a clinical setting consistent with ischemia. It is more sensitive and specific than conventional markers like CPK-MB and NT-Pro BNP. cTnT examination after 8 hr will provide the most helpful clue in the diagnosis of MI.

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