

Research Article

Evaluation of cardiac specific Troponin T as a specific and sensitive biomarker over Creatine Kinase-MB in Acute Myocardial Infarction patients - A correlation analysis study

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Abstract

The purpose of the study was to evaluate, cTnT as a sensitive and specific diagnostic and prognostic biomarker for myocardial damage among CKMB and LDH in Acute Myocardial Infarction cases by correlation analysis study. 50 patients of both sex (36-70 yrs.), with symptoms of acute myocardial infarction within 6 hours of onset were included in the study. Cardiac specific Troponin T, CKMB and LDH were measured at the time of admission. Descriptive statistics and Pearson correlation analysis were done. Our study showed a statistically significant positive correlation between cTnT and CKMB [r (48) = 0.708, and p <0.0001], between cTnT and LDH [r (48) = 0.740 and p <0.0001] and between CKMB and LDH [r (48) = 0.531 and p <0.0001]. cTnT with CKMB and LDH in AMI. We conclude with supporting the fact that cTnT estimation is sufficient as a specific and sensitive biomarker for Acute Myocardial Infarction diagnosis and prognosis over CKMB and LDH isoenzymes. Due to its sensitivity and practically perfect cardiac specificity, cTnT should be preferred over CK-MB for the detection of cardiac injury.

Keywords: Cardiac specific Troponin T (cTnT), Creatine kinase-MB (CKMB), Lactate dehydrogenase (LDH), Electrocardiogram (ECG), Acute myocardial infarction (AMI).

1. Introduction

Myocardial infarction (MI) is a major cause of death and disability worldwide. Myocardial injury is detected when blood levels of sensitive and specific biomarkers such as cTn or the MB fraction of creatine kinase (CKMB) are increased.⁽¹⁾ Cardiac troponin T (cTnT) originating exclusively from the myocardium [cardiac TnT, molecular weight (39.7 kD)] clearly differs from skeletal muscle TnT. As a result of its high tissue specificity, cTnT is a cardiac specific, highly sensitive marker for myocardial damage.⁽²⁾ cTnT increases approximately 3-4 hours after Acute Myocardial Infarction (AMI) and may persist up to 2 weeks thereafter.⁽³⁾⁽⁴⁾ In contrast to ST elevation myocardial infarction (STEMI), the diagnosis of non ST elevation myocardial infarction (NSTEMI) heavily relies on cardiac troponin result. Patients without elevated biomarker values can be diagnosed as having unstable angina.

cTnT is an independent prognostic marker which can predict the near, mid and even long term outcome of patients with acute coronary syndrome (ACS).⁽⁵⁾ Low concentrations of cTnT can be detected in clinically stable patients such as patients with ischemic or non-ischemic heart failure,⁽⁶⁾ patients with different forms of cardiomyopathy,⁽⁷⁾ renal failure,⁽⁸⁾ and diabetes.⁽⁹⁾ Myocardial cell injury leading to elevated cTnT concentrations in the blood can also occur in other clinical conditions such as myocarditis,⁽¹⁰⁾ heart contusion,⁽¹¹⁾ pulmonary embolism⁽¹²⁾ and drug-induced cardiotoxicity.⁽¹³⁾ Other diagnostic tests such as myoglobin, CK-MB, natriuretic peptide (NT-proBNP), placental growth factor (PIGF) and C-Reactive protein (CRP) can complement the diagnostic and prognostic information of cTnT in different indications.⁽¹⁴⁾

If cTn assay is not available, the best alternative is creatine kinase MB (CKMB). The CK-MB increase in plasma levels usually occur between 6 to 10 hours after the onset of infarction (in the absence of reperfusion / thrombolysis), peak at 24 hours and return to normal by 36 to 72 hours. CK-MB 2 isoform greater than 1.0 U/liter or a ratio of CK-MB2 to CK-MB1 greater than 2.5 has sensitivity for diagnosing MI of 46.4% at 4 hours and of 91.5% at 6 hours.

The aim of the present study was to evaluate the possibility of establishing cTn-T as an early, single, specific and sensitive biomarker for AMI over CKMB by correlation analysis study.

2. Materials and Methods

The correlation analysis study was carried out at Department of Biochemistry and Medicine in Dhanalakshmi Srinivasan Medical College, Perambalur, Tamil Nadu. Fifty patients of both sexes in the age group of 36-70 years (mean \pm SD = 54.3 \pm 10.46), with diagnosis of AMI were randomly selected for this prospective study. After detailed clinical examination, patients with myopericarditis, heart failure, pulmonary embolus, sepsis, cardiac contusion, cardiac surgery and renal disease were excluded from the study. Patients with symptoms of AMI of less than six hours were taken for study and at admission biomarkers like cardiac specific Troponin-T (cTnT), CKMB and lactate dehydrogenase (LDH) were estimated. Cardiac Troponin T was measured by a newly developed immunometric 1-step sandwich assay.⁽⁴⁾

2.1 Statistical Analysis

Descriptive statistics like mean and standard deviation (SD) were calculated. Pearson correlation analysis and non-parametric equivalent Spearman's rank correlation coefficient at 95% confidence of interval were done using SaIStat and Minitab English 15 statistical software.

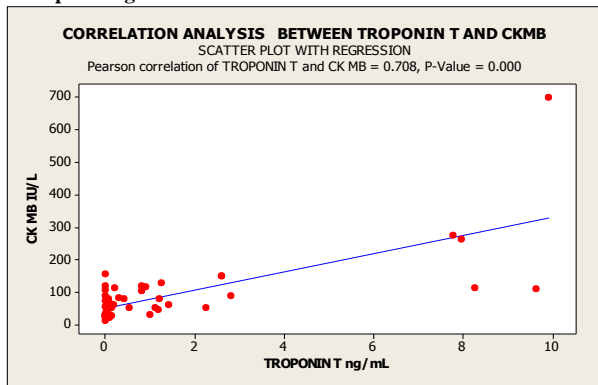
3. Results

Out of 50 AMI cases studied, 33 (66%) were STEMI and 17 (34%) were NSTEMI. cTnT (mean ± SD = 1.340 ± 2.609), CKMB (mean ± SD = 87.8 ± 103.6) and LDH (mean ± SD = 759.2 ± 702.7) values were significantly elevated.

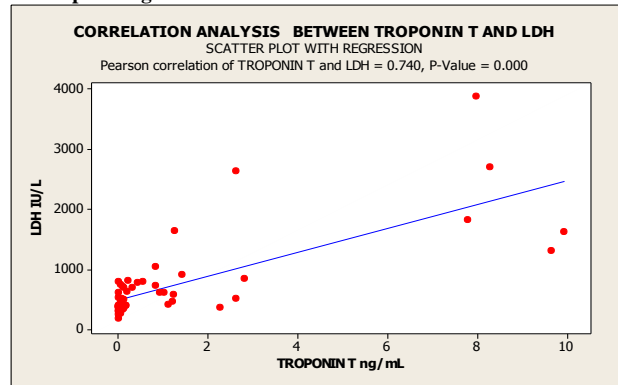
Table- 1 : Correlation analysis					
Variables	cTnT verses CKMB	cTnT verses LDH	CKMB Verses LDH	STEMI cTnT verses STEMI CKMB r(31)	NSTEMI cTnT verses NSTEMI CKMB r(15)
Pearson's correlation coefficient					
r(48) value	0.708	0.740	0.531	0.695	0.812
t value	6.942	7.618	4.342	5.385	5.393
p value	0.000000	0.000000	0.000073	0.000007	0.000075
Spearman's rank correlation coefficient					
rho(48) value	0.557	0.707	0.714	rho(31) 0.487	rho(15) 0.697
p value	0.000026	0.000000	0.000000	0.004039	0.001862

cTnT = Cardiac specific Troponin T, CKMB = Creatine kinase-MB, LDH = Lactate dehydrogenase

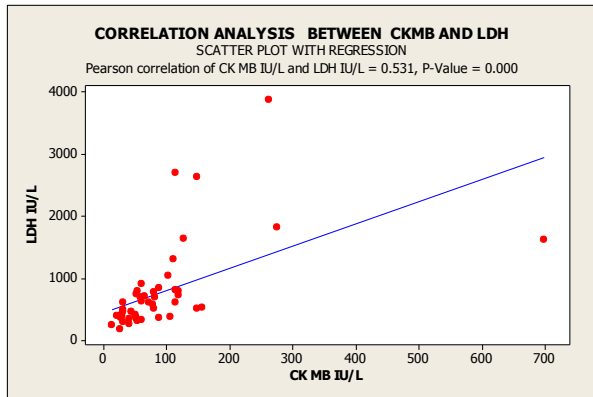
Scatterplot diagram 1: Positive correlation between cTn-T and CK MB



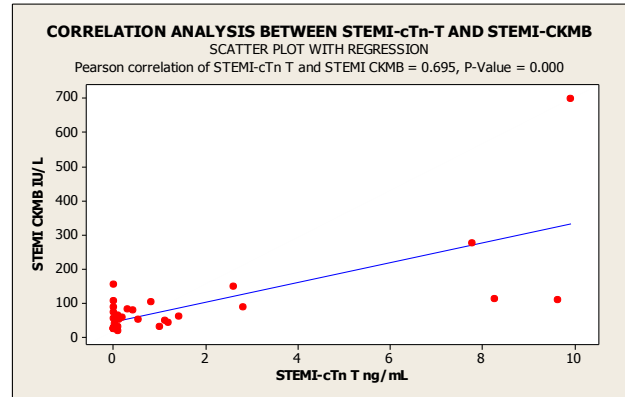
Scatterplot diagram 2: Positive correlation between cTn-T and LDH



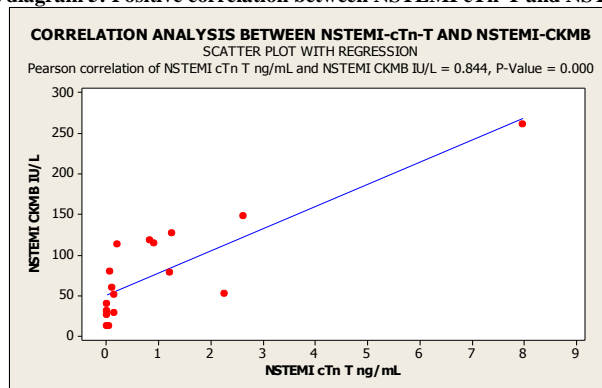
Scatterplot diagram 3: Positive correlation between CKMB and LDH



Scatterplot diagram 4: Positive correlation between STEMI cTn-T and STEMI CKMB



Scatterplot diagram 5: Positive correlation between NSTEMI cTn-T and NSTEMI CKMB



4. Discussion

In this study, we evaluated whether cTnT estimation alone is satisfactory as biomarker for diagnosis and prognosis of AMI by doing correlation analysis study. A statistically significant positive correlation was found between cTnT and CKMB [r (48) = 0.708, and p <0.0001] graph-1, between cTnT and LDH [r (48) = 0.740 and p <0.0001] graph-2 and between CKMB and LDH [r (48) = 0.531 and p <0.0001] graph-3, as shown in our table-1.

Furthermore, a statistically highly significant positive correlation was found between STEMI cTnT and STEMI CKMB [r (31) = 0.695 and p <0.0001] graph-4 and NSTEMI cTnT and NSTEMI CKMB [r (15) = 0.844 and p <0.0001] graph-5, as shown in our table-1.

Calculation of correlation analysis by non-parametric equivalent Spearman's rank correlation coefficient also showed the same result as Pearson's correlation coefficient analysis as shown in the table-1

Correlation analysis was also represented graphically by scatter diagram. In all the scatter diagrams, cTn-T value was taken on horizontal axis and CKMB and LDH values were taken on vertical axis. In all the scatterplot diagrams (1,2,3), almost all the points are concentrated on the arbitrary central linear line suggesting statistically significant linear relationship between increased cTn-T and increased CKMB and LDH respectively. Similar findings were also observed between STEMI cTn-T and STEMI CKMB and between NSTEMI cTn-T and NSTEMI CKMB as shown in our scatter diagrams 4 and 5 respectively.

In our study we found that, elevated levels of cTnT, CKMB and LDH showed a statistically significant positive correlation. Furthermore, a statistically significant positive correlation was also found between STEMI cTnT and STEMI CKMB and between NSTEMI cTnT and NSTEMI CKMB.

cTnT is cardiac specific, rapidly released after injury which remains for several days in circulation and can be rapidly assayed at relatively low cost. It is currently considered the best markers in diagnosing ACS. Cardiac specific troponin-T levels is used in risk stratification for a patient with chest pain that is not diagnosed with AMI at presentation. Elevations of cardiac specific troponin-T are especially significant when other markers are normal. These elevations predict higher risk of severe cardiac events in the coming month. In other patients with ACS, troponin elevations identify those who are at risk for cardiac events for up to six months. Troponin levels are used to plan medical and surgical treatments.

LDH and CK isoenzyme analyses have historically been used in humans to assess ischemia-induced cardiac injury. cTn is the analyte recommended for assessing injury associated with myocardial ischemia and is replacing CK-MB⁽¹⁵⁾ as its level returns to normal much faster than cardiac troponins levels. In reinfarction, CK-MB concentration rises again after the return to baseline levels so it can be measured when reinfarction is suspected. Currently, CK-MB results do not predict future adverse cardiac events and do not have any prognostic or risk stratification use. Measurement of LDH has remained as past test for diagnosis and prognosis of AMI.

We conclude with supporting the fact that cTnT estimation is sufficient as a specific and sensitive biomarker for AMI diagnosis and prognosis over CKMB and LDH isoenzymes. CKMB isoenzyme is less sensitive than cTnT as a biomarker for AMI and should be measured only as additional or as alternative test in the absence of cTnT test. Due to its enhanced sensitivity and practically perfect cardiac specificity, cTnT should be preferred over CK-MB for the detection of cardiac injury.

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