Original Article

Comparative Analysis of Sensitivity and Specificity of Creatinine Kinase MB and Cardiac Troponin I for the Diagnosis of Acute Myocardial Infarction

Nidhi Rohan Purandare[1], Astha Goyal[2], Sarita Shinde[3], Shilpa Jain[4]

Background : Early diagnosis is of crucial importance for the successful management of individuals with Acute Myocardial Infarction and is one of the leading causes of mortality and morbidity. We aimed to determine the sensitivity and specificity of two markers commonly used in our institution to diagnose patients with complaints indicative of Acute Myocardial Infarction.

Material and Methods : Patients admitted to the tertiary care center with complaints of chest pain were screened. Creatine Kinase Myoglobin Binding (CKMB) and Cardiac Troponin I (cTnI) were performed by following standard protocols. Depending upon the onset of chest pain subjects were divided into two groups, Group 1 : Within 24 hours of chest pain, Group 2 : Within 24-72 hours of chest pain. They were subdivided based on a diagnosis of MI. Results were used to calculate the specificity and sensitivity of CKMB, cTnI, and CKMB and cTnI together.

Results : Total of 368 patients were studied. Majority of them were >60 years of age. Of these, 133(36%) had confirmed diagnosis of MI. CKMB is more sensitive (82.19%) within 24 hours of MI but after 24 hours sensitivity decreases to (57.53%). CKMB is specific after 24 hours of MI (92.26%) compared to within 24 hours of MI (65.81%) whereas, cTnI is more specific (95.00%) after 24 hours.

Conclusion : For the diagnosis of Acute Myocardial Infarction (AMI), CKMB is more sensitive and cTnI is more specific, therefore it will be better if we perform cTnI rapid card test in combination with CKMB.

[*J Indian Med Assoc* 2024; **122(12):** 47-51]

***Key words* : CKMB, cTnI, Acute Myocardial Infarction, Sensitivity, Specificity.**

Myocardial infarction, the most serious side effect of Coronary Artery Disease, results from an abrupt thrombotic process that alters the perfusion balance between supply and demand within the coronary arteries[1,2]. Acute Myocardial Infarction (AMI) has a significant chance of being diagnosed early, which could save or extend a patient's life[3]. The American Heart Association advises that choosing the best treatment plans in the Emergency Department (ED) requires accurate 30-minute preferred turn around time for the identification of cardiac biomarkers from the complex biological fluid[4]. Cardiac biomarkers play an important role in the detection of Acute MI when the patient's history and Electrocardiogram (ECG) are non-diagnostic or equivocal[5]. Cardiac troponin-I (cTnI), the gold standard for detecting myocardial injury, is a highly specific biomarker to AMI[6].

Editor's Comment :

- There is a good probability that Acute Myocardial Infarction will be identified early, which could prolong or preserve a patient's life. When the patient's history and Electro-cardiogram are non-diagnostic or ambiguous, cardiac biomarkers play crucial role in identification of Acute Myocardial Infarction.
- The most accurate is cTnI, which is the gold standard for identifying myocardial damage, as CKMB and cTnI are often administered to patients with symptoms suggestive of acute myocardial infarction, this study looked into their sensitivity and specificity for the better diagnosis of Acute Myocardial Infarction.

Traditionally, patients presenting with chest pain had their myoc ardial health assessed using the enzymes such as Creatinine Kinase (CK), Lactate Dehydrogenase (LDH) and Aspartate Aminotransferase (AST). These indicators were sensitive to cellular death but not specific to myocardial damage. Later, serum myoglobin levels and the Myocardial Band (MB) isoform of Creatine Kinase (CK-MB) were used to improve diagnosis and increase specificity for heart injury. The most used biomarker for the identification of myocardial necrosis over the past two decades is the

Department of Biochemistry, Dr D Y Patil Medical College, Hospital & Research Centre, Pune, Maharashtra 411018
[1]MSc (Medical Biochemistry), Tutor
[2]MSc (Medical Biochemistry), Tutor and Corresponding Author
[3]PhD, Medical Biochemistry, Professor
[4]MD (Biochemistry), Professor and Head, Department of Biochemistry, Government Medical College Baroda, Gujarat 390001
Received on : 26/09/2023
Accepted on : 16/05/2024

assessment of serum troponin levels[7]. This study sought to investigate the sensitivity and specificity of CKMB and cTnI for the diagnosis of AMI because they are frequently performed in patients with complaints indicative of AMI.

Materials and Methods

This retrospective study was performed at the SSG Hospital, Medical College Baroda between the months of December, 2018 and April, 2019. Patients who complained of chest pain were evaluated based on pre-determined criteria.Patients who underwent CKMB and cTnI between 24 to 72 hours of experiencing chest discomfort were included. They were managed according to standard protocol. Those who agreed to participate signed an informed written consent. CKMB and cTn I were done within 24 hours of the chest discomfort to calculate sensitivity, specificity, predictive value of positive test and negative test of these markers. Ethical Clearance was not applicable as this was the retrospective study done for poster presentation at the 15th Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine Congress (APFCB) in 2019 and it was not mandatory at that period.

Thorough medical history of the individual with CKMB and cTnI data was obtained. CKMB and cTnI was performed within 24 hours of onset of chest pain and between 24 to 72 hours of chest pain by Immuno-Inhibition by blend of monoclonal antibody and chromatographic immunoassay fast card test respectively.

Depending upon the final diagnosis, patients were divided into two groups.

i) Group 1: Within 24 hours of chest pain
ii) Group 2: Within 24-72 hours of chest pain

They were further subdivided based on onset of chest pain.

i) Patients with confirmed diagnosis of MI (n=133)
ii) Patients without MI (n=235)

Statistical Analysis :

Data of CKMB and cTnI of all MI positive and MI negative patients were collected and

Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of test (NPV) were calculated using following formula;

Sensitivity = TP/ (TP+FN)*100

Specificity = TN/ (TN+FP)*100

Predictive Value of Positive test (PPV) = TP/ (TP+FP)*100

Predictive Value of Negative test (NPV) = TN/ (FN+TN)*100

Observation and Results

A total 368 patients were enrolled with the complaint of chest pain in emergency. Majority of them were >60 years of age. The Age and Gender distribution is shown in Table 1.

In our study, we found that the complaint of chest pain was more in male as compared to females. Also the complaint of chest pain increased with the age, subjects upto 40 years were lower compared to subjects more than 60 years.

Of the enrolled patients, 133 had confirmed diagnosis of MI. CKMB and cTnI were performed in these subjects and the results were plotted in 4x2 table.

Table 2 represents the values of these tests within 24 hours of onset and Table 3 represents the values of these tests within 24 to 72 hours on onset.

Table 2 shows subjects within 24 hours of onset of chest pain; only 73 were with MI positive and 155 were MI negative. Out of these CKMB found positive in 113 subjects whereas in 115 subjects CKMB was negative. In addition to this cTnI found positive in 54 subjects and negative in173 subjects.

Table 3 shows only 60 were with MI positive and 80 were MI negative. Out of these CKMB found positive in 85 subjects wereas in 55 subjects CKMB was negative. In addition to this cTnI found positive in 19 subjects and negative in121 subjects.

Further, we calculated the sensitivity and specificity performed in both study Groups and represented in Table 4.

Table 4 shows the comparision of sensitivity, specificity, PPV and NPV of CKMB and cTnI within 24 hours of MI and within 24-72 hours of MI with 95% of CI.

Fig 1 shows that CKMB is more sensitive (82.19%) within 24 hours of MI but after 24 hours the sensitivity decreases to (57.53%). In addition to this CKMB is specific after 24 hours of MI (92.26%) compared to within 24 hours of MI (65.81%). On other hand cTnI is not sensitive but more specific (95.00%) after 24 hours.

Discussion

Myocardial infarction is the main cause of

Table 1 — *Age and Gender Distribution*

Age	Males	Females
Upto 40 years	9	3
40-50 years	23	18
51-60 years	34	28
> 60 years	136	117
Total (n=368)	202	166

Table 2 — *Group 1 - Number of subjects with MI positive and MI negative within 24 hours onset of Chest pain*

	Onset	CKMB>24 IU/L (TP)	CKMB<24 IU/L (FN)	cTnI Positive (TP)	cTnI Negative (FN)
MI Positive n=73	Within 24 hours	60	13	42	31
		CKMB>24 IU/L (FP)	CKMB<24 IU/L (TN)	cTnI Positive (FP)	cTnI Negative (TN)
MI Negative n=155	Within 24 hours	53	102	12	143

MI : Myocardial Infraction, ICCU : Intensive Coronary Care Unit,
CKMB : Creatine Kinase Myoglobin Binding, cTnI : Cardiac Troponin I, TP : True Positive,
FP : False Positive, TN : True Negative, FN: False Negative

Table 3 — *Group 2 - Number of subjects with MI positive and MI negative within 24-72 hours of onset of chest pain*

	Onset	CKMB>24 IU/L (TP)	CKMB<24 IU/L (FN)	cTnI Positive (TP)	cTnI Negative (FN)
MI Positive n=60	24-72 hours	38	22	15	45
		CKMB>24 IU/L (FP)	CKMB<24 IU/L (TN)	cTnI Positive (FP)	cTnI Negative (TN)
MI Negative n=80	24-72 hours	47	33	4	76

MI : Myocardial Infraction, ICCU : Intensive Coronary Care Unit,
CKMB : Creatine Kinase Myoglobin Binding, cTnI : Cardiac Troponin ITP : True Positive,
FP : False Positive, TN : True Negative, FN: False Negative

morbidity and mortality Worldwide. An acute ST-Elevation Myocardial Infarction (STEMI) affects more than 3 million people annually, while non-ST-elevation Myocardial Infarction (NSTEMI) affects more than 4 million. NSTEMI and unstable angina are identical. Cardiovascular indicators, however, are not increased[10-12]. The WHO states that at least two of the following three criteria must be met in order to diagnose MI : (1) a history of chest discomfort of the ischemia variety (2) progression on successive electrocardiograms (3) changes in the serum cardiac marker levels. The examination of serial cardiac indicators is currently the cornerstone of these diagnostic criteria[13]. The Acute Myocardial Infarction consequences peak in the first few hours[14]. Early MI diagnosis and treatment are essential for preventing myocardial damage and maintaining heart function[15]. Cardiac troponin and creatine kinase-MB isoform are two popular biomarkers used to diagnose Acute Myocardial Infarction.

Cytoplasmic CK is a M and/or B subunit-containing dimer that associates to generate the isoenzymes CK-MM, CK-MB and CK-BB[16]. Following myocardial injury, serum total CK activity and CK-MB concentration rise together, beginning to climb 4-6 hours after the damage, reaching peak serum concentrations after 12-24 hours, and reverting to baseline after 48-72 hours. Compared to serum total CK, which may be increased in many diseases where skeletal muscle is injured, serum CK-MB is far more specific for myocardial injury[17]. Therefore, CK should only be used in conjunction with other more precise cardiac markers to diagnose myocardial damage.[18]

The regulation of striated and cardiac muscle contraction is carried out by the troponin complex components; TnC, TnI, and TnT[16]. Troponin C is not highly selective for myocardial damage since its isoforms in skeletal and cardiac muscle are similar[19,20]. Troponin I has not been isolated from skeletal muscle and is very selective for the cardiac muscle. It is the excellent marker of myocardial damage because of its extreme specificity[21]. After myocardial damage, they are released into the bloodstream 6-8 hours later, reach their peak at 12-24 hours and then remain high for 7-10 days[22]. The only drawback is the late clearance of cTn, which makes it challenging to detect a recurrence of myocardial infarction[23].

Finding the best and clear cardiac biomarker for evaluating AMI has always been an actively debated issue in research. Despite being more cardiospecific, new diagnostic assays were shown to have lower diagnostic efficacy when compared to the gold standard CK-MB[8]. The purpose of the current study

Table 4 — *Sensitivity and specificity of CKMB and cTnI in subjects within 24 hours of onset of Chest pain and within 24-72 hours of onset of chest pain*

Statistics	Within 24 hours				24-72 hours			
	CKMB	95% CI	cTnI	95% CI	CKMB	95% CI	cTnI	95% CI
Sensitivity	82.19%	71.47% to 90.16%	57.53%	45.41% to 69.03%	63.33%	49.90% to 75.41%	25.00%	14.72% to 37.86%
Specificity	65.81%	57.77% to 73.23%	92.26%	86.87% to 95.94%	41.25%	30.35% to 52.82%	95.00%	87.69% to 98.62%
PPV	53.10%	43.48% to 62.55%	77.78%	64.40% to 87.96%	44.71%	33.91% to 55.89%	78.95%	54.43% to 93.95%
NPV	88.70%	81.45% to 93.84%	82.18%	75.68% to 87.56%	60.00%	45.91% to 72.98%	62.81%	53.56% to 71.42%

CKMB : Creatine Kinase Myoglobin Binding, cTnI : Cardiac Troponin IPPV : Positive Predictive Value, NPV : Negative Predictive Value

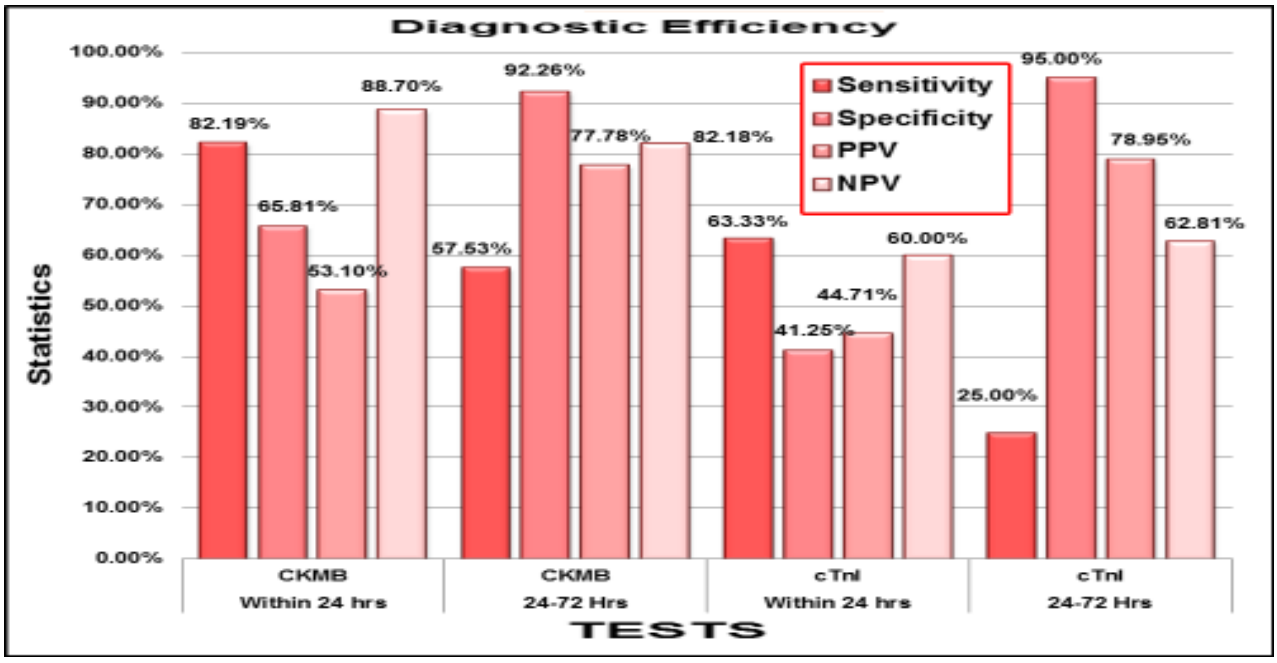

Fig 1 — Comparison of sensitivity, Specificity, PPV, and NPV between CKMB, cTn I and Combined CKMB with cTnI

is to evaluate the diagnostic performance of cardiac Troponin-I and CKMB for detecting acute MI in patients as soon as they arrive in the emergency room.

In 2000, Cardiac Troponin took CK-MB's status as the preferred biomarker for identifying myocardial infarctions[24]. The early clearance aids in the identification of reinfarction, is the only advantage of CKMB over Troponin. To diagnose myocardial infarction, the serum troponin level and CK-MB fraction level are therefore measureds[25].

In this study, the serum troponin level is measured for the diagnosis of myocardial infarction, the level of the CK-MB fraction is measured. We found CKMB is more sensitive (82.19%) while cTnI is more specific (92.26%). Compare to the study done by PS Mahalakshmi and PS Babu found that for cTnI the sensitivity and specificity was 96% and 98%[7] which was higher than our results and for CKMB the sensitivity and specificity was 62% and 68% which was lower than our results. Sharbari Basu,et.al. found that cTnI was 100% specific[6], in our study it is 92.25% specific while CK-MB was a more sensitive marker in diagnosis of AMI.

Conclusion

In developing countries early diagnosis is crucial since AMI is the primary cause of mortality and morbidity. Serum cardiac biomarkers analysis is currently the mainstay of MI diagnosis. A serum cardiac marker should be very sensitive and highly specific in order to accurately diagnose MI.

When compared to cTnI, the current investigation discovered a statistically extremely significant rise in CKMB levels in participants who had MI at the time of admission to the emergency department. High specificity (92.26%) and PPV (77.78%) were displayed by cTnI. It is the earliest marker for the confirmation and exclusion of acute MI within 24 hours after the infarction, in addition to the specificity increases after 24-72 hours of MI (95.00%).

In conclusion, It was found that CKMB, when compared to cTnI, is a more sensitive marker and a superior diagnostic accuracy for the identification of AMI, especially in the first 24 hours after an episode of AMI whereas cTnI is more specific.

References

1 Amsterdam EA, Wenger NK, Brindis RG, Casey Jr DE, Ganiats TG, Holmes Jr DR, *et al* — 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; **130(25):** 2354-94.

2 Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, *et al* — Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 2019; **139(10):** e56-28.

3 Motamed H, Mohammadi M, Tayebi Z, Rafati Navaei A — The diagnostic utility of creatine kinase-MB versus total creatine

phosphokinase ratio in patients with non-ST elevation myocardial infarction from unstable angina. *SAGE Open Medicine* 2023; **11:** 20503121221148609.
4 Goswami PP, Deshpande T, Rotake DR, Singh SG — Near perfect classification of cardiac biomarker Troponin-I in human serum assisted by SnS2-CNT composite, explainable ML, and operating-voltage-selection-algorithm. *Biosensors and Bioelectronics* 2023; **220:** 114915.
5 Rains MG, Laney CA, Bailey AL, Campbell CL — Biomarkers of acute myocardial infarction in the elderly: troponin and beyond. *Clinical Interventions in Aging* 2014; **11:** 1081-90.
6 Basu S, Rani UP, Srinivasan AR — Association of creatine kinase MB and troponin I with electrocardiographic changes in acute myocardial infarction. *Biomed Research* 2009; **20(2):** 84-6.
7 Petimani MS, Babu PS — Study of cardiac troponin-i as a diagnostic marker in comparision with creatine KINASE-MB in myocardial infarction.
8 Daubert MA, Jeremias A — The utility of troponin measurement to deyect myocardial infarction : review of the current findings. *Vascular Health and Risk Management* 2010; 691-9.
9 Warell DA, Cox TM, Firth JD — Clinical cardiology. In: Oxford textbook of medicine 4th edition. *Oxford University Press New York* 2003; **2:** 388.
11 Nascimento BR, Brant LCC, Marino BCA, Passaglia LG, Ribeiro ALP — Implementing myocardial infarction systems of care in low/middle-income countries. *Heart* 2019; **105(1):** 20-6.
11 Barberi C, van den Hondel KE — The use of cardiac troponin T (cTnT) in the postmortem diagnosis of acute myocardial infarction and sudden cardiac death: A systematic review. *Forensic Sci Int* 2018; **292:** 27-38.
12 Alaour B, Liew F, Kaier TE — Cardiac Troponin - diagnostic problems and impact on cardiovascular disease. *Ann Med* 2018; **50(8):** 655-65.
13 Alexander JH, Sparapani RA, Mahaffey KW, Deckers JM, Newby KL, Ohman ME, *et al* — Association between minor elevations of creatine kinase-MB level and mortality in patients with acute coronary syndromes without ST-segment elevation. *JAMA* 2000; **283:** 347-53.
14 Baheti R, Laddha P, Gehlot RS — Value of Troponin-T test in the diagnosiss of acute myocardial infarction. *J Indian Academy of Clinical Medicine* 2002; **3(1):** 55-8.
15 Daubert MA, Jeremias A — The utility of troponin measurement to deyect myocardial infarction : review of the current findings. *Vascular Health and Risk Management* 2010; 691-9.
16 Kemp M, Donovan J, Higham H, Hooper J — Biochemical markers of myocardial injury. *British Journal of Anaesthesia* 2004; **93(1):** 63-73.
17 Homburg JJ, Friedman DL, Perryman MB — Metabolic and diagnostic signi®cance of creatine kinase isoenzymes. *Trends Cardiovasc Med* 1991; **1:** 195±200
18 Jaffe AS, Ravkilde J, Roberts R Its time for a change to a troponin standard. *Circulation* 2000; **102:** 1216±20.
19 Lewandrowski K, Chen A and Januzzi J — Cardiac markers for myocardial infarction. A brief review. *Am J Clin Pathol* 2002; **118 (Suppl 1):** S93-S99.
20 Ruseva A — Laboratory diagnosis of acute myocardial infarction. *Trakia J Sci* 2005; **3:** 8-14.
21 Higgins JP and Higgins JA — Elevation of cardiac troponin I indicates more than myocardial ischemia. *Clin Invest Med* 2003; **26:** 133-47.
22 Tucker JF, Collins RA, Anderson AJ, Hauser J, Kalas J, Apple FS — Early diagnostic efficiency of cardiac troponin I and Troponin T for acute myocardial infarction. *Acad Emerg Med* 1997; **4:** 13-21.
23 Mythili S, Malathi N — Diagnostic markers of acute myocardial infarction. *Biomedical Reports* 2015; **3(6):** 743-8.
24 Alpert JS, Thygesen K, Antman E, Bassand JP — Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000; **36:** 959-69. 10.1016/S0735-1097(00)00804-4.
25 Gerhardt W, Katus H, Ravkilde J — S-troponin T in suspected ischemic myocardial injury compared with mass and catalytic concentrations of S-creatine kinase isoenzyme MB. *Clin Chem* 1991; **37:** 1405-11.