ORIGINAL RESEARCH PAPER

Volume-7 | Issue-9 | September-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION OF SERUM CARDIAC TROPONIN -I (cTnI) AS A MORE SENSITIVE MARKER THAN SERUM CKMB IN THE EARLY DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION (AMI)

General Medicine

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ABSTRACT

Cardiac troponin-I (cTnI) is more sensitive serum marker than CKMB in the early diagnosis of acute myocardial infarction (AMI). A prospective clinical study consisting of 100 AMI patients was under taken to evaluate the Cardiac troponin-I (cTnI) levels on admission with acute chest pain to ICCU. It seems reasonable for clinicians to measure cardiac troponin-I (cTnI) in patients with suspected AMI which could result in the more cost-effective use of intensive care facilities.

Background: The diagnosis of AMI was confirmed only in 30-50% of cases at the time of admission to hospitals. This was because, ECG changes were seen only in about half of the AMI cases and approximately ¼th of patients with AMI did not present with classic chest pain and the event could go unrecognized. Therefore, in majority of patients the clinicians must obtain serum cardiac marker measurement for early diagnosis of AMI. Because earlier diagnosis gives the opportunity to the patients to receive the benefits of thrombolytic and other therapy.

Material and Methods: A total 100 patients with history of chest pain suggestive of acute myocardial infarction were included in the study. All the patients were tested for:

a) CK-MB by using immuno-inhibition methodology

b) cTnI by using a rapid immuno-chromatographic method

c) Serial ECG changes.

In proved 80 AMI cases, in samples collected in between 6-24 hours of chest pain and 42 AMI cases in samples collected in between 6-8 hours of chest pain, the sensitivity of cTnI and CK-MB was compared.

Results: Out of 80 AMI cases, the cTnI was positive in 48 cases (60% sensitivity) and CKMB was positive in 36 cases (45% sensitivity) in samples collected between 6-24 hours of chest pain. Whereas out of 42 AMI cases, cTnI was positive in 26 cases (62% sensitivity) and CKMB was positive in 19 cases (45% sensitivity) in samples collected between 6-8 hours of chest pain.

Conclusion:

- Cardiac troponin-I (cTnI) was more sensitive serum marker than CKMB in the early diagnosis of acute myocardial infarction (AMI).
- It seems reasonable for clinicians to measure cardiac troponin-I (cTnI). In patients with suspected AMI which could result in the more costeffective use of intensive care facilities.
- In the future, further improvements in analytical performance may open additional diagnostic windows.

KEYWORDS

Acute Myocardial Infarction; Cardiac Troponin-i; Creatine Kinase Mb; Electrocardiography.

INTRODUCTION :

Cardiovascular diseases are at present the leading causes of death in the developed countries. Ischemic heart disease is the cause of 25-30% of deaths in most industrialized countries[1].

At the beginning of the 20th century, cardiovascular diseases (CVD) accounted for less than 10% of all deaths worldwide. At the beginning of the 21st century, they accounted for nearly half of all the deaths in the developed world and 25% in the developing world. By 2020, it is predicted that the diseases will claim 25 million lives annually and that coronary heart disease (CHD) will surpass infectious diseases as the world's number one cause of death and disability[2].

Acute myocardial infarction (AMI) is one of the most common diagnoses in hospitalized patients in industrialized countries. In the United states, approximately 6.5 lakh patients experience a new AMI and 4.5 lakh experience a recurrent AMI each year. The early mortality rate from AMI is 30% with about half of the deaths occurring within 1 hour of the event from ventriculr tachyarrhythmia. Although the mortality rate after admission for AMI has declined by 30-% over the past decades, approximately 1 of every 25 patients who survive the initial hospitalization die in the first year after AMI[3].

The reasons to provide an earlier, more rapid and specific diagnosis are compelling:

Only about 15% of patients presenting to the emergency room with chest pain and suspected AMI are ultimately found to have MI as subseaquently documented by objective means[4].

1. High cost of unnecessary hospital admission, estimated at $ 12 billion annually in Us[5].
2. Fibrinolysis (reperfusion) within the first 1 or 2 hours of chest pain, results in preservation of ventricular function[6] and reduce mortality by 90% compared with little if any reduction in mortality at 10 to 12 hours[7].
3. Fibrinolytic therapy in unstable angina increased death and infarction[8]. Thus exclusion of infarction would also allow early administration of more appropriate therapy for unstable angina viz., antithrombin and antiplatelet therapy[9].
4. Even a 0.5% incidence of intracranial bleeding complicating thrombolytic therapy is unacceptable in individuals without AMI
5. Early detection of coronary reocclusion and reinfarction might prevent as many as 1/5th of the hospital deaths among patients who have received thrombolysis.

The classic World Health Organization (WHO) criteria for the diagnosis of AMI require that at least two of the following three elements be present:

1. A history of ischemic type of chest discomfort.
2. Evolutionary changes on serially obtained ECG tracings, and
3. A rise and fall in serum cardiac markers[10].

In hospital admitted patients, diagnosis of AMI according to WHO criteria was confirmed in only 30-50% cases. ECG changes are seen only in about ½ of AMI cases on presentation. Approximately ¼th of patients with AMI do not present with classic chest pain and the event would go unrecognized[11].

Therefore, in majority of patients the clinicians must obtain serum cardiac marker measurements for diagnosing AMI. The gold standard for diagnosis of MI has been an elevated serum level of creatinine kinase – myocardial band (CK-MB), the cardiac-specific isoenzyme of CK[12]. However, elevated CK-MB may not detect all myocardial necrosis. In patients who die suddenly after severe or silent episodes of ischemia, autopsies frequently reveal micronecrosis that was not reflected in routine CK-MB measurement.

New cardiac marker, the Troponin-I with superior sensitivity and specificity for myocardial damage and greater ability to risk stratify

patients with ischemic myocardial necrosis is now challenging the role of CK-MB. Monoclonal antibody based assays have been developed that are specific for the cardiac isoform of troponin-I[12]. Using such assays, data are now available confirming that troponins (I) can identify myocardial micronecrosis even when an AMI diagnosis has been excluded – according to the conventional definition[12].

In response to these and other issues, a new definition of MI was proposed in September 2000[12], which emphasizes the use of cardiac troponin (I) as the preferred marker of myocardial necrosis in the context of ischemic symptoms in routine clinical practice.

Thus, when comparing the diagnostic sensitivity of cTnI versus CK-MB for AMI, the cTnI has got the capability of detecting the minor myocardial damage (MMD) even in patients without increases of CK-MB. The present study is undertaken to compare the diagnostic sensitivity of cTnI versus CK-MB in AMI patients. Because earlier diagnosis of AMI gives the opportunity to the patients to receive the benefits of thrombolytic and other therapy.

AIMS AND OBJECTIVES:

The present study aims to know that serum Cardiac Troponin-I is more sensitive marker than serum CPK-MB in early diagnosis of acute myocardial infarction (AMI).

MATERIALS AND METHODS:

The study "Evaluation of Serum Cardiac Troponin-I (cTnI) as a More Sensitive Marker than Serum CK-MB in the Early Diagnosis of Acute Myocardial Infarction" was carried out in Government General Hospital ,Kurnool during the period from June 2015 to May 2017.

The study was undertaken with an aim to study that serum cardiac troponin-I (cTnI) is more sensitive than serum CK-MB in early diagnosis of acute myocardial infarction (AMI).

Selection of Patients: The study was conducted on patients admitted with history of chest pain suggestive of AMI as diagnosed by WHO criteria to medicine ward of Government General Hospital, Kurnool.

Sample Size: The sample size includes 100 patients with history of chest pain suggestive of AMI, selected by simple random method. Of these, 80 patients were diagnosed as having AMI by using WHO criteria after exclusion of patients having acute pericarditis, severe heart failure, acute myocarditis, cardiac trauma, skeletal muscle disease and/ or trauma, chronic renal failure.

EXCLUSION CRITERIA:

1. Acute pericarditis
2. Severe heart failure
3. Acute myocarditis
4. Cardiac trauma
5. Chronic renal failure
6. Skeletal muscle disease and/ or trauma
7. Hematologic malignancies

OBSERVATION AND RESULTS:

Total 100 cases with history of chest pain suggestive of acute myocardial infarction admitted to Government General Hospital, Kurnool ICCU department were studied. Of these, 80 were proved of having acute myocardial infarction (both STEMI and NSTEMI). Our study observations among the proved AMI cases are as follows:

TABLE-1: Age And Sex Wise Distribution Of Acute Myocardial Infarction Cases(n=80)

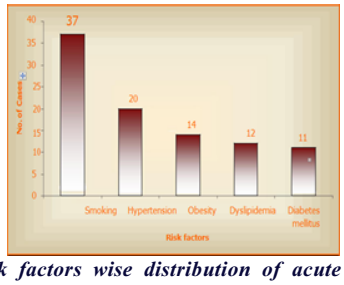
Age group (Yrs)	Male		Female	
	Number	Percent	Number	Percent
31 – 40	7	11	1	5.8
41 – 50	20	32	5	29.4
51 – 60	23	36.5	6	35.2
61 – 70	7	11	3	17
71 – 80	4	6.3	2	11.7
81 – 90	2	3.1	--	--
Total	63	79	17	21

The maximum number of cases of acute myocardial infarction were found in age group 51-60 years followed by 41-50 years in both males and females. In the present study, 63% of the patients were male and 17% females. 8 patients had acute myocardial infarction with age <40 years called young acute myocardial infarction.

TABLE-2: Risk Factors Wise Distribution Of Acute Myocardial Infarction

Risk factors	Number of Cases	Percentage
Smoking	37	46.2
Hypertension	20	25
Dyslipidemia	12	15
Obesity	14	17.5
Diabetes mellitus	11	13.7

It can be observed that smoking was the major risk factor followed by hypertension and least was diabetes mellitus.



Graph 1: Risk factors wise distribution of acute myocardial infarction cases

TABLE-3: Distribution Of Acute Myocardial Infarction Cases According To Site Of Heart Involved

Site wise AMI type	Number	Percentage
Anterior wall acute myocardial Infarction	48	60.00
Inferior wall acute myocardial Infarction	21	26.20
Global acute myocardial infarction	8	10.0
Right ventricular acute myocardial Infarction	3	3.70

In table-3, maximum number of cases were having anterior wall acute myocardial infarction followed by inferior wall acute myocardial infarction. Least was right ventricular myocardial infarction.

GRAPH-2: Distribution Of Acute Myocardial Infarction Cases According To Site Of Heart Involved

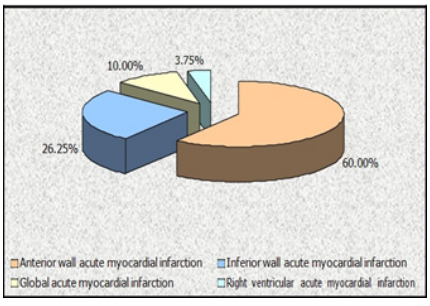


TABLE-4: ST Elevation MI versus Non-ST Elevation MI Cases

Type of AMI	Number of Cases	Percentage
STEMI	70	88.00
NSTEMI	10	12.00
Total	80	100.00

Table-4 shows that maximum number of acute myocardial infarctions were ST elevation myocrdial infarctions.

GRAPH 3: ST Elevation MI versus Non-ST Elevation MI Cases

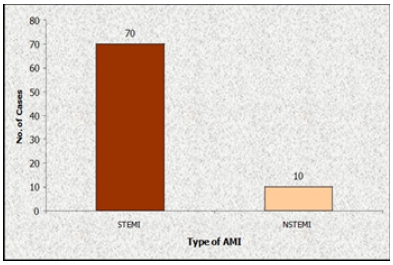
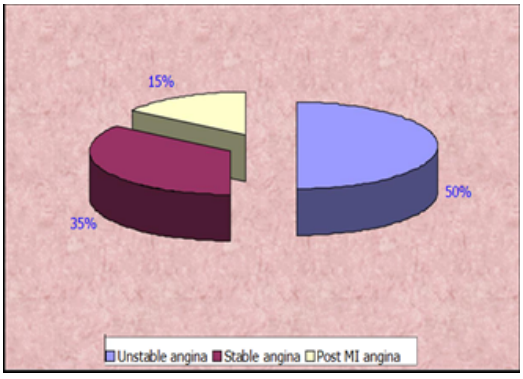


TABLE-5: Distribution of Non-Acute Myocardial Infarction Cases

Type of Non- AMI cases	Number of Cases	Percentage
Stable angina	7	35.00
Unstable angina	10	50.00
Post MI angina	3	15.00
Total	**20**	**100.00**

Table-5 shows that among non-AMI cases majority were unstable angina cases, followed by stable angina and least by post-myocardial infarction angina.



GRAPH 4: Distribution Of Non-acute Myocardial Infarction Cases

TABLE-6: Cases Admitted Within 12 Hours From Onset Of Chest Pain

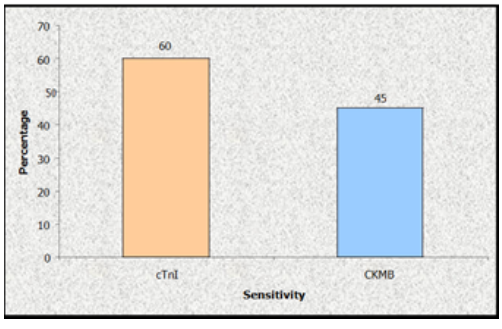
No. of cases admitted within 12 hours of chest Pain	Total AMI cases	Percentage
65	80	80.00

Table-6 shows that majority 80% of the AMI patients were admitted to the ICCU department within 12 hours of onset of chest pain.

TABLE-7: Overall Sensitivity Of CKMB And Ctni In Proved Ami Cases Admitted In Between 6-24 Hours Of Chest Pain

	Total No. Of AMI cases	CKMB/ cTnI positive cases	Sensitivity Percentage
CKMB	80	36	45.00
cTnI	80	48	60.00

Table-7 shows that cardiac troponin-I is more sensitive than CK-MB in overall cases admitted in between 6 hours to 24 hours from the onset of chest pain.



Graph 5: Overall Sensitivity Of CKMB And Ctni In Proved Ami Cases Admitted In Between 6-24 Hours Of Chest Pain

TABLE-8: CKMB And Ctni Sensitivity In Acute Myocardial Infarction Patients (falling Within 6-8 Hours Of Chest Pain Onset)

	Total No. of AMI cases from 6-8 hours of onset of chest pain	CKMB/ cTnI positive cases	Sensitivity (Percentage)
CKMB	42	19	45.00
cTnI	42	26	62.0

TABLE-8 Shows That From 6-8 Hours Of Onset Of Chest Pain To Admission, Ctni Is More Sensitive Than CKMB.

TABLE-9: CKMB and cTnI Sensitivity In Acute Myocardial Infarction Cases Admitted After 12 Hours Of Chest Pain Symptom

	Total No. of AMI cases after 12 hours of onset of chest pain	CKMB/ cTnI positive cases	Sensitivity (Percentage)
CKMB	15	9	60
cTnI	15	12	80

Table-9 shows that after 12 hours of onset of chest pain, the sensitivity of both the cardiac biomarkers increases but more in favour of cTnI.

TABLE -10: Ctnl Sensitivity In Acute Myocardial Infarction Cases Where Ckmb Is Normal

Total No. of AMI cases	No. of positive cTnI cases where CKMB is normal	Sensitivity (Percentage)
80	28	35.00

Table-10 shows that in 35% of cases where CKMB is normal, the cTnI detects the AMI cases indicating its sensitivity

TABLE-11: Ctni Sensitivity In Unstable Angina Cases, Where Ck-mb Is Negative

Total CKMB negative UA cases	No. of cTnI positive cases in CKMB negative cases	Percentage of detection of MMD
8	8	100.00

Table-11 shows that 8 out of 8 UA cases with negative CKMB values had cTnI positive test indicating MMD.

DISCUSSION :

Acute myocardial infarction (AMI) is the cause of 25-30% of deaths in most industrialized countries1. By 2020 it is predicted that the ischemic heart disease will surpass infectious disease as the world's number one cause of death and disability[2].

Decades of observational studies have verified excess MI risk in men compared with women.

TABLE 12: Gender Comparison

Study	Male	Female
Kanitz et al study	81	19
Present study	79	21

TABLE 13: Gender Comparison

Study	Male	Female
Kanitz et al study	72	28
Present study	79	21

In the present study 79% of acute myocardial infarction patients were male and 21% were females.

TABLE 14: Gender Comparison

Study	Male	Female
Vyas et al study	76	24
Present study	79	21

In the present study 79% of acute myocardial infarction patients were male and 21% were females.

Smoking:

Smoking accelerates atherosclerosis in both sexes and at all ages and increases the risk of thrombosis, plaque instability, myocardial infarction and death. In Tanajura et al study, the prevalence of smoking was 81%.

TABLE 15: Comparison Of Prevalence Of Smoking

Study	Smoking prevalence
Tanajura et al study	81
Present study	46

TABLE 16: Comparison Of Prevalence Of Smoking

Study	Smoking prevalence
Zagreb et al study	51
Present study	46

Zagreb et al study 51% smoking prevalence is seen in present study it is 46%.

A wealth of epidemiologic data support a relationship between hypertension and atherosclerotic heart disease, more recent studies also show a reduction in CHD risk by antihypertensive therapy. In Tanajura et al study, the prevalence of hypertension was 22%.

TABLE 17: Comparison of prevalence of hypertension

Study	Hypertension prevalence
Tanajura et al study	22
Present study	25

In Zagreb et al study Hypertension prevalence 49% and present study it is 25%.

TABLE 18: Comparison of prevalence of hypertension

Study	Hypertension prevalence
Zagreb et al study	49
Present study	25

Abnormalities in plasma lipoprotein and derangements in lipid metabolism rank as the most firmly established and best understood risk factors for AMI. In Tanajura et al study, the prevalence of dyslipidemia was 16%.

TABLE 19: Comparison Of Prevalence Of Dyslipidemia

Study	Dyslipidemia prevalence
Tanajura et al study	16
Present study	15

Diabetes mellitus is a chronic heart disease risk equivalent; most patients with diabetes mellitus dies of atherosclerosis and its complications. In Tanajura et al study, the prevalence of diabetes mellitus was 14%.

TABLE 20: Comparison Of Diabetes Prevalence

Study	Diabetes prevalence
Tanajura et al study	14
Present study	13.7

In the present study, the prevalence of smoking was 4%, hypertension 25%, dyslipidemia 15% and diabetes mellitus 13.7%.

Changes in cardiac troponins and CK-MB:

According to Mario D'ecosta et al about 80% of the acute myocardial infarction cases were admitted to the ICCU ward within 12 hours from the onset of chest pain.

The present study also shows the same (80%) of acute myocardial infarction cases who were admitted within 12 hours of chest pain.

In Mario D'Costa et al study, the overall peak performance of cTnI testing in samples received within 24 hours of admission indicated high sensitivity of 97%. In the same study, the sensitivity for cTnI was 79% and for CKMB was 44% in AMI patients first specimen obtained at admission.

TABLE 21: Comparison single CKMB and cTnI Sensitivity

Study	Single CKMB Sensitivity	Single cTnI sensitivity
Mario D Costa et al study	44	79
Present study	45	60

A single CK-MB value in emergency department patients with acute chest pain had a sensitivity for detecting AMI of 34%, a single value of cTnI had a sensitivity of about 40%.

Zurich SW et al found using a single troponin-I determination, that 46% of patients with confirmed MI had an abnormal cTnI and normal CKMB initially.

TABLE 22: Comparison Of Ctni Sensitivity

Study	cTnI Sensitivity
Zurich S W et al study	46
Present study	60

In our study, a single CKMB and cTnI value in ICCU ward patients with history of acute chest pain had a sensitivity of 45% and 60% respectively for detecting acute myocardial infarction.

Our study also showed that cTnI sensitivity increased (60% to 62%) and CKMB sensitivity remained same (45%) in patients admitted in between 6-8 hours of chest pain. This indicates that cTnI is more sensitive than CKMB in earlier AMI cases.

Single values of CKMB and cTnI drawn more than 12 hours after the onset of symptoms had sensitivities for AMI in the range of 70-90%.

In the present study, the single value of CKMB and cTnI had the sensitivities of 60% and 80% drawn more than 12 hours after the onset of chest pain symptoms respectively.

TABLE 23: Comparison Of Sensitivity Of Ckmb And Ctni In Less Than 12 Hours And More Than 12 Hours

Sensitivity	6 to 8 Hrs		>12Hrs	
	CTnI	CKMB	cTnI	CKMB
	60- 62%	45%	80%	60%

In a study by Kliemam S et al, 31% of the patients with normal CKMB (mass) had elevated cTnI levels, whereas in our study, 35% of the patients were having elevated cTnI levels with normal CKMB values.

TABLE 24: Comparing Patients With Normal Ckmb With Increased Ctni

Study	Normal CKMB with increased cTnI
Kliemam S et al study	31%
Present study	35%

Adams JE 3rdet al6 (1993), evaluated cardiac Troponin I as a marker with high specificity for cardiac injury. They concluded that elevations of cTnI are highly specific for myocardial injury. Use of cTnI should facilitate distinguishing whether elevations of MBCK are due to myocardial or skeletal muscle injury.

Adams JE 3rd et al7(1994), done a study on comparable detection of acute myocardial infarction by creatine kinase MB isoenzyme and cardiac troponin I. They concluded that cTnI and CK-MB had statistically indistinguishable diagnostic accuracies for the detection of acute myocardial infarction.

Brogan GX Jret al8 (1997), done a study on evaluation of a new assay for cardiac Troponin I vs Creatine kinase-MB for the diagnosis of acute myocardial infarction. They concluded cTn-I was as sensitive and specific for AMI as was CK-MB in ED patients who presented within 24 hours of symptom onset. However, cTn-I was more sensitive in patients who presented > or = 24 hours after symptom onset. Elevations of either marker within 6 hours of symptom onset predict an increased risk of complications and/or need for interventions.

Shazib Pervaiz et al9 (1997), done a comparative analysis of cardiac Troponin I and Creatine Kinase-MB as markers of acute myocardial infarction. They concluded that cTnI is an excellent marker for detecting and ruling out AMI, because it has better specificity and a wider diagnostic window than the accepted standard, CK-MB.

Durdi Qujeq10 (1999), done a study on rapid diagnosis of acute myocardial infarction. Consecutive 150 patients admitted to the coronary care unit was studied. They concluded that measurement of CTn-I accurately detects MI in patients and should facilitate the diagnosis and management of such patients.

Ross G et al11 (2000), done a study on Troponin I-sensitivity and specificity for the diagnosis of acute myocardial infarction. They concluded that when a troponin I level greater than 0.6 ng/mL was used as a positive value, compared to CK-MB and ECG using either time zero or time 6 hours, the sensitivity was 84% and specificity was 81%. When troponin I greater than 2.0 ng/mL was used to define a positive test, the sensitivity was 85% and specificity was 91% when compared to CK-MB and ECG.

Kiran R. Bagaleet al12(2014), done a study on Role of CK-MB and Troponin-I in Diagnosing Non-ST-Elevation Myocardial Infarction. They concluded that Troponin-I can identify the minimal cardiac damage which will be useful for the physician to start immediate intervention.

Brogan GX Jr et al8 (1997), done a study on evaluation of a new assay for cardiac Troponin I vs Creatine kinase-MB for the diagnosis of acute

myocardial infarction. Patients who had elevations in either CK-MB or cTn-I within 6 hours of symptom onset were at increased risk for cardiovascular complications and/or interventions (CK-MB, OR 5.8; cTn-I, OR 6.3). So they concluded cTn-I was as sensitive and specific for AMI as was CK-MB in ED patients who presented within 24 hours of symptom onset. However, cTn-I was more sensitive in patients who presented > or = 24 hours after symptom onset. Elevations of either marker within 6 hours of symptom onset predict an increased risk of complications and/or need for interventions.

Shazib Pervaiz et al9 (1997), done a comparative analysis of cardiac Troponin I and Creatine Kinase-MB as markers of acute myocardial infarction. They concluded that cTnI is an excellent marker for detecting and ruling out AMI, because it has better specificity and a wider diagnostic window than the accepted standard, CK-MB.

Janice Zimmerman et al13(1999), done a diagnostic marker cooperative study for the diagnosis of myocardial infarction. They found that with each marker as the diagnostic standard, CK-MB subforms and myoglobin remained the most sensitive for early diagnosis. So they concluded that the CK-MB subform assay alone or in combination with a troponin reliably triages patients with chest pain and should lead to improved therapy and reduced cost.

Bock JL et al 14(1999), done an evaluation of CK-MB isoform analysis for early diagnosis of myocardial infarction. They concluded that analysis of CK-MB by high-voltage electrophoresis is an effective method for rapid diagnosis of MI, with the isoform analysis enhancing early sensitivity.

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