Original Article

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Ischemia Modified Albumin in Early Diagnosis of Acute Coronary Syndromes

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Abstract

Background: Acute coronary syndromes (ACS) pose a diagnostic challenge in patients with unpredictable baseline ECGs or without evidence of myocardial necrosis. Its early diagnosis is of utmost importance as ACS has a high mortality. The present study was conducted to know the role of Ischemia Modified Albumin (IMA) as a Cardiac Marker in the early Diagnosis of ACS. **Subjects and Methods:** A cross-sectional study was conducted in 86 patients presenting with chest pain of less than 3hours. A 12-lead ECG was recorded, and a blood sample was taken for IMA and cardiac troponin T(cTnT). Results of all the parameters alone and in combination, were correlated with the final hospital diagnosis and analysed. **Results:** IMA was found to be abnormal among 72.1% of the patients. IMA had a sensitivity of 81.58% and a specificity of 83.33% which was found to be high when compared with other parameters. The combination of IMA, ECG, 2D ECHO, cTnT, and CKMB had a sensitivity of 100% and a specificity of 16.67%. **Conclusion:** The present study showed that IMA is a potential diagnostic biomarker for ACS. Further studies are required to support the present findings.

Keywords: Acute coronary syndromes, Ischemic Modified Albumin, Cardiac Marker.

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Introduction

Cardiovascular disease (CVD) is single-handedly responsible for the largest number of deaths worldwide. According to the World Health Organization (WHO), in 2008, over 17 million people died from CVD, representing 30% of all global deaths, Coronary heart disease (CHD) and strokes account for over two-thirds of all CVD mortality.[1] The average age of having a first heart attack is 66 years for a man and 70 years for a woman.[2]

ACS is a spectrum of clinical presentation causing acute myocardial ischemia in which there is evidence of myocardial injury or necrosis.[3] ACS refers to a spectrum of clinical presentations ranging from ST-segment elevation myocardial infarction (STEMI), non–ST-segment elevation myocardial infarction (NSTEMI), and unstable angina. The diagnosis of ACS is missed in approximately 2% of patients, leading to a two-fold increase in short-term mortality of patients who are mistakenly discharged when compared to patients who are admitted to the hospital.[4]

The traditional clinical variables for diagnosing MI are 12 lead ECG, serum cardiac biomarkers, cardiac imaging, and nonspecific indices of tissue necrosis and inflammation. The 12 lead ECG remains a critical tool in diagnosis and follow-up with its accurate identification of the infarct vessel and predicts the amount of myocardium at risk and guides in decisions regarding the urgency of revascularization. If the initial ECG is non-diagnostic and the patient remains symptomatic, serial ECGs should be obtained every 15-30 minutes to detect sudden ischemic ST-segment changes.[5]

A practical approach in a patient presenting with ischemic symptoms (after an ECG has been reviewed) should include measuring CK-MB and or troponin I.[6] CK-MB has lower sensitivity and specificity for myocardial injury as a small amount is also found in skeletal muscle tissue. cTnT and I have greater specificity of myocardial necrosis than troponin C, which is also found in skeletal muscle tissue.[6,7] ECHO helps in identifying regional wall-motion abnormalities, valvular dysfunction, risk stratification, and assessment of left and right ventricular systolic function.

IMA is a recently identified biomarker of transient myocardial ischemia. IMA is a serum albumin in which the N-terminus is chemically modified, which was originally observed by Barr-OR et al, 2001.[8] These modifications are caused by free radical-induced by ischemia, reperfusion or acidosis.

Previous studies have shown that IMA levels rise within minutes after cardiac ischemia and have high negative predictive value and hence can be used as a cardiac biomarker of myocardial ischemia in emergency.[9] It is already been licensed by the US Food and Drug Administration for the diagnosis of suspected myocardial ischemia.

Considering the high mortality and no traditional "gold standard" clinical variables for the diagnosis of ACS, IMA a new biomarker, is used in the present study for early diagnosis of MI.

Subjects and Methods

A cross-sectional study was conducted after approval of institutional ethics committee. Patients with chest pain of less than 3 hours duration visiting MS Ramaiah Medical College hospitals between September 2012 to August 2013 were included in the study. Pregnant women, patients of acute mesenteric ischemia, acute renal failure, peripheral vascular disease, and brain ischemia were excluded.

A 12-lead ECG was recorded and a blood sample was taken for IMA and cTnT in each patient. ECGs with ST-segment elevation or depression >0.1mv or T wave inversion >0.2mv in two or more contiguous leads were considered positive. Equivocal or unpredictable ECGs such as left bundle branch block, paced rhythm, and persistent ST elevation after previous Acute Myocardial Infarct were considered negative. Cardiac troponin T(cTnT)>0.05ng/ml is considered positive.[9] Enzyme-linked Immunoabsorbent Assay Kit was used for measuring IMA. The underlying principle is, cobalt added to serum does not bind to the NH2 terminus of IMA, leaving more free cobalt to react with dithiothreitol and forms a darker color in samples from patients with ischemia. IMA values > 85 U/ Ml are considered as positive for cardiac ischemia. Angiogram with >70% stenosis in any major epicardial vessel is positive. Results of all the parameters alone and in combination, were correlated with final hospital diagnosis and analyzed.

Sample size estimation was done using N Master software considering the sensitivity of IMA of 85%,[10] the precision of ±2, and confidence interval of 95% the sample worked out to be 86. Tools of the screening test like sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the testing were calculated.

Results

Out of 86 patients, <40 years were 8 (9.3%), 40-60years were 38 (44.2%) and >60years were 40 (46.5%). 48 (55.8%) were Males.

With the clinical history, it was found that 58 (67.4%) were diabetic, 59 (68.6%) were hypertensive, 27 (31.4%) were smokers and 40 (46.5%) were with obesity.

39 (45.3%) of the patients presented with typical chest pain and 47 (54.7%) presented with atypical chest pain.

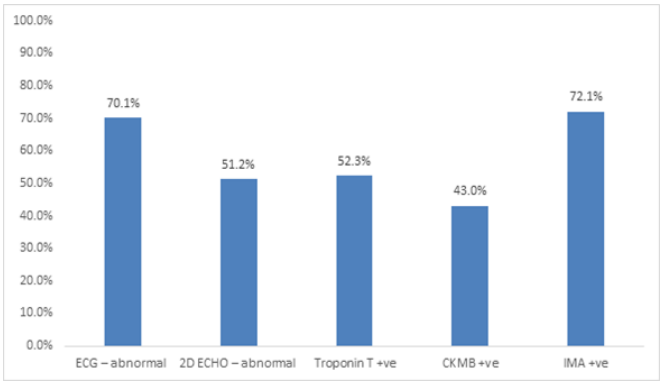

Figure 1: Abnormal investigation findings.

IMA was found to be abnormal among 72.1% of the patients. [Figure 1]

IMA has a sensitivity of 81.58% and a specificity of 83.33% which is high when compared with the other parameters. The combination of IMA, ECG, 2D ECHO, cTnT, and CKMB has a sensitivity of 100% and a specificity of 16.67% [Table 1,2].

Discussion

CK-MB and cardiac troponin-T are currently referred to as key cardiac biomarkers for ACS diagnosis due to high cardiac specificity. However, neither of them can identify ACS until more than 4hours after the onset of the chest pain in most cases. Thus, IMA would act as a newer available cardiac biomarker with superior performance in the diagnosis of reversible ischemia in early-stage ACS.

In the present study, the majority of them were males (55.8%) and the majority were more than 60years of age. In patients who presented within 3 hours of chest pain, it was found that IMA had a sensitivity of 81.58%, a specificity of 83.33% and an accuracy of 81.02%. For ECG, sensitivity was 58.11%, specificity was 25% and accuracy was 53.48%. For 2D ECHO, sensitivity was 56.76%, specificity was 83.33% and accuracy was 60.47%. For cTnT, sensitivity was 55.41%, specificity was 66.67% and accuracy was 56.98%. For CKMB, sensitivity

Table 1: Comparison of various investigations with CAGfindings.

	True positive	False positive	False negative	True negative
ECG - abnormal	43	9	31	3
2D ECHO - abnormal	42	2	32	10
Troponin T +ve	41	4	33	8
CKMB +ve	31	6	43	6
IMA +ve	60	2	14	10
IMA + ECG	66	9	8	3
IMA + 2D ECHO	66	3	8	9
IMA + Trop T	67	6	7	6
IMA + ECG + 2D ECHO + Trop T + CKMB	74	10	0	2

Table 2: Screening parameters of various diagnostic methodsand markers alone and in combination.

	Sensitivity	Specificity	PPV	NPV	Accuracy
ECG - abnormal	58.11%	25%	82.69%	8.82%	53.48%
2D ECHO - abnormal	56.76%	83.33%	95.45%	23.81%	60.47%
Troponin T +ve	55.41%	66.67%	91.11%	19.51%	56.98%
CKMB +ve	41.89%	50%	83.78%	12.24%	43.02%
IMA +ve	81.58%	83.33%	96.88%	41.67%	81.02%
IMA + ECG	89.19%	25%	88%	27.27%	80.23%
IMA + 2D ECHO	89.19%	75%	95.65%	52.94%	87.21%
IMA + Trop T	90.54%	50%	91.78%	46.15%	84.88%
IMA + ECG + 2D ECHO + Trop T + CKMB	100%	16.67%	88.10%	100%	88.37%

was 41.89%, specificity was 50% and accuracy was 43.02%. With combined tests, sensitivity was 100%, specificity was 16.67% and accuracy was 88.37%.

In a study done by Sinha MK et al,[11] the Sensitivity of ECG was 45%, cTcT was 20%, IMA+cTnT was 92%, IMA+ECG was 90% and IMA+ECG+cTnT was 95%. Specificity of IMA+ECG was 43%, IMA+nTcT was 44%, and IMA+ECG+cTnT was 42%.

A study by Chun-jian et al showed that the sensitivity of IMA was 93.0% while the sensitivity of CK- MB was 67.5% and the sensitivity of cTnT was 69.3%.[12] This study also demonstrated that the sensitivity of IMA was superior to conventional biomarkers cTnT and CK-MB. Similarly, Gururajan et al also found that IMA had a maximum sensitivity of 87% in their study.[13] Anwaruddin et al, study showed that the sensitivity of IMA was 97.0% and the sensitivity of CK-MB was 23.9%.[14]

Conclusion

The present study showed that Ischemia modified albumin is a potential diagnostic biomarker for ACS. Significantly more ACS patients were recognised at the presentation by IMA than other markers alone. Further studies are required to support the present finding.

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