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Original Article

Value of Non-Invasive Markers of Coronary Artery Patency after Thrombolytic Therapy in Acute Myocardial Infarction

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Abstract:

Acute myocardial infarction is a potentially life-threatening condition and patient may die or become disabled in the prime of life. This hospital based observational study was conducted in medicine and cardiology department of Faridpur Medical College Hospital from 25th March 2015 to 24th September 2015 among patients with acute myocardial infarction to see the value of non-invasive markers (ST resolution and CK-MB peaking) in the detection of reperfusion after thrombolysis. Total 100 consecutive patients with their first myocardial infarction undergoing thrombolytic therapy were included in the study. Study shows maximum number of patients 49 (49%) were between 51-60 years' age group, next 26 (26%) were between the age group of 61-70 years. Total 78% were male and 22% were female & majority of the acute myocardial infarction were inferior (57%). Present study showed that 86% of patients succeed to reperfusion and 14% fail to reperfusion. Blood samples were taken on admission and 90 minutes after thrombolytic therapy. The times at which the concentrations of the CK-MB markers peaked significantly at 90 minutes in patients of reperfused group (88%) than in those of not reperfused (12%). These results emphasize the release of these markers when reperfusion is established.

Key words: Acute myocardial infarction, Thrombolytic therapy, Non-invasive markers of coronary artery patency.

Introduction:

Acute coronary syndrome is a devastating disease because an otherwise healthy person may die or become disabled without warning. Heart disease has already reached epidemic proportions in poorer countries also. If the affected individuals 40 years old or below, the tragic consequences are catastrophic. As life expectancy continues to increase, cardiologists will observe an ever

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increasing number of elderly patients with acute myocardial infarction[1]. Myocardial infarction (MI) is a common form of coronary heart disease. Nine modifiable risk factors are associated with incident MI and explain more than 95% of the population attributable risk (PAR) of acute MI among women and men from all regions of the world. Over the last few years, intravenous thrombolysis has become the standard therapeutic approach for patients with myocardial infarction. The reduction in short and long-term mortality rates caused by thrombolytic therapy was demonstrated in several large scale clinical trials. With intravenous administration of newer thrombolytic agents, coronary artery patency rates of 70% to 80% have been reported[2-8].

Intravenous thrombolytic therapy for acute myocardial infarction yields maximal benefit if there is early and sustained restoration of Thrombolysis in Myocardial Infarction (TIMI) in the infarct-related artery (IRA). In acute myocardial infarction treated with intravenous streptokinase, a simple measurement of increased serum concentrations of CKMB mass, cardiac troponin T or myoglobin at 60 and 90 minutes can accurately predict failure to achieve TIMI grade 3 flow in the IRA at 90 min[9].

However, failure of complete reperfusion by 90 min after thrombolytic administration has been demonstrated in 46% of patients treated with the best of the current thrombolytic regimens[10]. Because clinical assessment of thrombolytic efficacy is unreliable, a rapid noninvasive method of detecting failure of complete reperfusion of the infarct-related artery could be of considerable assistance, by identifying the patients who might benefit from further reperfusion strategies, such as rescue angioplasty. Because the kinetics of release and clearance of the conventional biochemical markers of myocardial necrosis are not sufficiently sensitive to monitor reperfusion within the first 60 to 90 min noninvasively, attempts have been made to improve their sensitivity and specificity by means of multiple samples and the construction of time–activity curves. These methods are complex and time consuming. The use of newer serum markers of myocyte necrosis, such as CK, CK-MB, myoglobin, and cardiac troponin T, could simplify the task. Levels of these proteins rise rapidly in the serum after successful reperfusion therapy of MI. The present study sought to assess the value of non-invasive markers as predictors of coronary artery patency after thrombolytic therapy in acute myocardial infarction.[11,12]

A single non-invasive marker to evaluate reperfusion would be of significant clinical benefit. Various studies have assessed different cardiac marker proteins as indicators of reperfusion.Peaking of CK-MB at 90 minutes has been demonstrated in successful reperfusion but occurs too late to be of value in the selection of patients for further invasive treatment. In recent years, a wide range of rapid assays for cardiac marker proteins have been developed. The aim of this study was to compare directly the release kinetics of cardiac markers for which rapid assays are available: CK-MB throughout the course of acute myocardial infarction[13].

Materials and Methods:

This was a cross sectional, observational study. Sample was selected from the population by purposive sampling technique. Detail demographic data were collected from the subject and recorded in structured case report form. Clinical examination and relevant investigations were done meticulously. Total 100 consecutive patients with their first myocardial infarction undergoing thrombolytic therapy were prospectively included in the study between 25th March and 24th September 2015 at Faridpur Medical College Hospital (FMCH). All patients gave informed consent to the study, which had been approved by the ethical committee of the FMCH. The pre-structured Case Record Form (CRF) filled up, case definition of operational variable had been described. Then data were entered into computer with the help of SPSS version 16. Thrombolytic treatment was given to any patient presenting within 12 hours of the onset of symptoms with clinical and electrocardiographic evidence of acute myocardial infarction-that is, presenting with typical angina chest pain for at least 30 min but not greater than 24 hours and with ST segment elevation on electrocardiogram (ECG) of greater than 0.1 mV in two limb leads or 0.2mV in two pericardial leads, and who did not have a contraindication to thrombolysis. Streptokinase was used as thrombolytic agent with a doses of 1.5 million/U and were given to all patients. Blood sample was collected before giving thrombolytic therapy and 90 minutes after thrombolytic therapy. CK-MB was assayed from the blood sample and the same time ECG also performed when the blood sample was collected. Then peaking of CK-MB level at 90 minutes and resolution of ST segment elevation of ECG were correlated. Normal range of CK-MB is <25.0 unit/L, 25-30 unit/L is suspected and >30 unit/L considered positive.

The mean change in ST elevation at 90 minutes after thrombolytic treatment was expressed as a percentage reduction from the initial value (fractional change), as demonstrated by 50% resolution of the ST segment elevation[14].

The result was presented in tables in proportion. Z test of proportion was done to analyze the data. Level of significance was 0.05.

Results:

Incidence of acute MI gradually increased with rising of age. In case of male and female 51 to 60 years was highest incidence, following that incidence of disease predominant in female patient. The average age of female patients (51-60 years) was higher than males (41-60 years) (Figure 1)

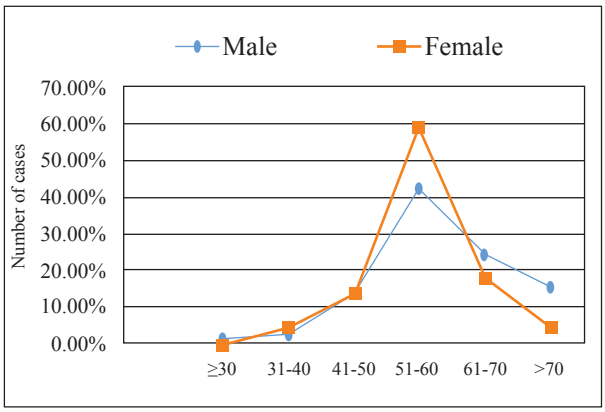

Figure-1: Line chart showing the frequency and incidence of disease with age variation (n=100)

Majority of the acute myocardial infarction were anterior (57%) (Figure 2).

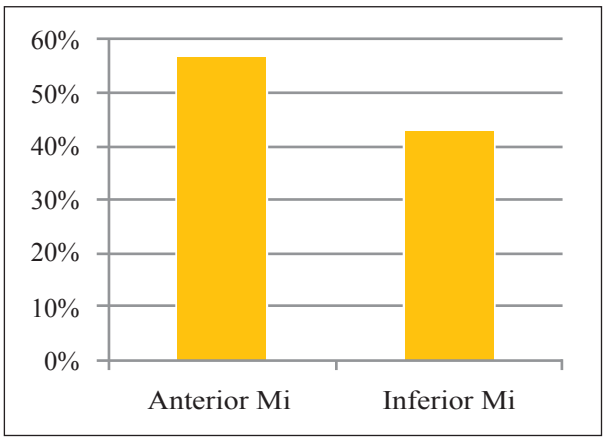

Figure-2: Types of acute myocardial infarction (n=100)

Table I showed that 86% of patients succeed to reperfusion and 14% fail to reperfusion.

Table I: ECG changes after thrombolytic therapy and pattern of coronary artery patency (n=100)

ST changes and pattern of Infarct Reperfusion	Number of patients (%)
≥50% resolution of the ST segment (Reperfused)	86 (86)
≤50% of the ST segment (Not reperfused)	14 (14)

The concentrations of the CK-MB markers peaked significantly at 90 minutes in patients of reperfused group (88%) than in those of not reperfused (12%). These results emphasis the release of these markers when reperfusion is established (Table II).

Table II: CK-MB level after thrombolytic therapy and pattern of coronary artery patency (n=100)

CK-MB level	Number of patients (%)
Peaking (Reperfused)	88 (88)
Not peaking (Not perfused)	12 (12)

CK-MB was peaking in reperfused group. Among the 88 patients of peaking CK-MB, 84 (95.45%) correlates with ST segment normalization, but 4 (4.54%) patients not correlated. The mean (range) percentage change in ST segment normalization in patients who reperfused after thrombolytic treatment was 80 (50-100) %, while in those who failed to reperfuse the mean (range) percentage change was only 4 (0-25%) (Table III).

Table III: Comparison of non-invasive markers (ST resolution and CK-MB peaking) in the detection of reperfusion after thrombolysis in acute myocardial infarction (n=100)

ECG changes	CK-MB level			
	Reperfused (n=88)	Not perfused (n=12)	*Z value	p value
Reperfused (n=86)	84 (95.45%)	2 (16.66%)	3.1	0.001
Not perfused (n=14)	4 (4.54%)	10 (83.33%)		

*Z test of proportion was done to analyze the data. Level of significance was 0.05.

Discussion:

Augusto R et al[15] revealed that Infarcts in the inferior wall occurred in 50% of the females and in 55.3% of the males (p=0.53), while Q-wave infarcts had a similar distribution in both sexes (81.5% in females and 82.4% in males; p=0.87). In our study male preponderance may be due to cultural attitude of our society that the females are not generally brought to the hospitals or as the disease is of old age and our female population lives shorter than their male counterparts.

The ideal non-invasive marker of reperfusion must indicate as early as possible whether reperfusion has occurred to permit maximum benefit to be derived from further interventional procedures. In addition to the presence of the marker in concentrations related to the reperfusion status of the patient, it is essential that rapid assay methods are available for the marker. Otherwise, the benefits of early detection will not be realized. The mean change in ST elevation at 90 minutes after thrombolytic treatment was expressed as a percentage reduction from the initial value (fractional change), as demonstrated by 50% resolution of the ST segment elevation (operational definition). Present study showed that 86% of patients succeed to reperfusion and 14% fail to reperfusion. Blood samples were taken on admission and 90 minutes after thrombolytic therapy. The times at which the concentrations of the CK-MB markers peaked significantly at 90 minutes in patients of reperfused group (88%) than in those of not reperfused (12%). These results emphasize the earlier release of these markers when reperfusion is established. Determination of the time to peak concentration of any marker, however, involves measurement of the concentration of the marker by serial blood sampling until the decline in plasma concentration is observed. Such a procedure does not lend itself to early indication of the reperfusion status of the patient. As an alternative, the rate of change in the serum concentration of some markers shortly after administration of thrombolytic agent has been examined. Increases in CK-MB mass of 2.2- fold over baseline within 90 min or increases in CK-MB activity (mean (SE)) of 48 (36) U/l in the first hour after treatment were indicative of reperfusion in other studies[14,16,17].

The predictability of patency of the infarct-related artery assessed by means of two noninvasive easily obtainable markers was prospectively examined in 82 patients undergoing thrombolysis for their first myocardial infarction. Positive noninvasive markers were defined as follows: 1) peak (at 90 minutes) creatine kinase (CK-MB) activity; 2) ≥50% reductions in ST segment elevation. Separate analysis of each marker revealed the following respective values for sensitivity, specificity and positive and negative predictive value regarding prediction of coronary artery patency: CK-MB prediction: 95.45%, 83.33%, 97.67% and 71.42%. Lavin F[15] et al demonstrated that peak times of the four markers, namely CK, CK-MB mass, myoglobin, and troponin T, were significantly earlier when reperfusion occurred. Several studies have assessed the clinical usefulness of the time to peak concentration of these markers as indicators of reperfusion. One study showed that the time of peak serum concentration of myoglobin, CK, and CK-MB activity predicted reperfusion with diagnostic efficiencies of 93, 89, and 88%, respectively[18]. In another study found that the time to peak CK activity in combination with two clinical markers, resolution of ST segment elevation, and occurrence of arrhythmia could predict the occurrence of reperfusion with 100% sensitivity 90% specificity[19]. These results suggest that an early peaking CK-MB marker and fractional change of ST elevation showing myocardial injury is a useful non-invasive marker of reperfusion. The use of a more complex classification increased the sensitivity of the test at the expense of its specificity.

Conclusion:

Myocardial infarction is foremost causes of morbidity, mortality. It is recommended that provision of proper health care support, early detection of risk factors with prevention, can reduce the incidence of Acute Coronary Syndrome. Reliable determination of reperfusion status is only possible by coronary angiography. This technique is frequently either impractical or unavailable in an emergency setting. Standard non-invasive criteria, such as rapid relief of chest pain, rapid normalization of ST segment elevation, and occurrence of reperfusion arrhythmia, have been accepted as non-invasive signs of reperfusion. Our study suggested that non-invasive marker (CK- MB) to evaluate reperfusion would be of significant clinical benefit after thrombolysis.

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