Value Of Non-Invasive Markers Of Coronary Artery Patency After Thrombolysis In Acute Myocardial Infarction In Pakistani Population*

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Summary:

Non-invasive method of monitoring reperfusion of infarct-related artery can be used to identify the majority of patients with inadequate reperfusion. These non-responsive patients may get benefit from mechanical revascularization. Percent (%) ST change of > 50 resolutions at 90 minutes of thrombolytic treatment provides a method that is both specific and sensitive. CKMB peak within 12 hours gives high degree of sensitivity but low specificity. Reperfusion arrhythmias are poor indicator of reperfusion having low sensitivity.

Introduction

Thrombolytic therapy has been a major advance in the management of acute myocardial infarction. Its introduction in late 1970s and early 1980s has revolutionized the treatment of patients with AMI, reducing mortality by a magnitude exceeding all previous therapeutic efforts. Thrombolytic therapy works by lysing infarct artery thrombosis and achieving reperfusion, therapy reducing infarct size, preserving left ventricular function and improving survival[1-4]. Although 60-70% of treated patients can be successfully reperfused[5], thrombolytic therapy fails in a substantial proportion. These non-responsive patients have a significantly high mortality rate and may therefore be candidates for emergency angioplasty or coronary artery bypass surgery. Therefore it is crucial to document reperfusion in a timely fashion. While coronary angiography is the "gold standard" to document reperfusion, this is an invasive procedure associated with small but defined risk for the patients and facilities to perform coronary angiography is not widely available in our country in public sector hospital. Reliable assessment of coronary artery patency after thrombolytic treatment would allow appropriate triage of patients to invasive intervention. Rescue angioplasty is beneficial in some patients with failure of recanalization after thrombolytic therapy[6].

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The non-invasive markers that are readily available and highly accurate are most desirable. The traditional non-invasive markers of infarct-related coronary artery patency after thrombolysis include, rapid resolution of ST segment elevation, reperfusion arrhythmias, early appearance and peaking of cardiac enzyme level, sudden resolution of conduction disturbance on ECG, early pyrophosphate uptake by scintigraphy and response of chest pain to therapy.

The purpose of the study is to establish the value of non-invasive markers for coronary artery patency after thrombolytic treatment in AMI in Pakistani population.

TABLE - 1

Reperfusion Rate, Relation with Age

Age Group (years)	No. of Cases (n = 68)	TIMI Grade-II, III (reperfused) (n = 39)	Percentage
21 - 25	01	01	100
26 - 30	01	01	100
31 - 35	08	03	37.50
36 - 40	13	08	61.53
41 - 45	16	12	75.00
46 - 50	08	03	37.50
51 - 55	08	03	37.50
56 - 60	11	07	63.63
61 - 65	02	01	50.00

Reperfusion Arrhythmias

In 10 patients with TIMI grade-II, III flow episode of accelerated idioventricular rhythm were documented. Two patients with inferior wall MI demonstrated sinus bradycardia. Reperfusion arrhythmias were observed in 12 (31%) patients with documented patient infarct-related artery (TIMI grade-II, III). Three patients with TIMI grade-0, 1 flow demonstrated accelerated idioventricular rhythm. Overall, 75% of patients showing one of the defined reperfusion arrhythmias had a patent infarct-related artery. However, 69% of patients without reperfusion arrhythmias also had successful reperfusion accounting low predictive value (Table-6), so according to these value reperfusion arrhythmias as a marker for reperfusion has sensitivity 31%, specificity 86%, positive predictive value of 75%, and negative predictive value 48%.

In combined analysis of three non-invasive markers, sensitivity for prediction of coronary artery reperfusion decreases (Table-7) because only 31% of patients having reperfused infarct-related artery developed reperfusion arrhythmic. Combined analysis of CKMB peak and ST elevation setting improved the sensitivity to 89%. These two markers have specificity, positive predictive value and negative predictive value of 62%, 76% and 82% respectively.

TABLE - 6

Reperfusion Arrhythmias

	TIMI-II, III (n = 39)	TIMI-0, 1 (n = 29)	Total
Arrhythmias observed	12 (31.00%)	4 (14.00%)	16
Arrhythmias not observed	27 (69.00%)	25 (86.00%)	52
Total	39	29	68

Sensitivity :: 31.00%
Specificity :: 86.00%

Positive predictive value :: 75.00%
Negative predictive value :: 48.00%

Discussion

The study documents the usefulness of the non-invasive marker of reperfusion after thrombolytic treatment in AMI. Use of percent (%) ST changes as diagnostic test provides a method with sufficient specificity and sensitivity to help identify non-reperfused patients who could benefit from cardiac catheterization with adjunctive intracoronary mechanical recanalization to restore infarct-related artery patency. The result of the study indicates the importance of using each patient as his own control to compare any change in ST segment elevation to the baseline value rather observing a change in absolute numbers of millimeters. The study revealed that percent (%) ST change of $\geq$ 50% resolution at 90 minutes after start of thrombolytic treatment provided a method that is both specific and sensitive (76% and 85% respectively).

Various studies, performed to evaluate the changes in CKMB after thrombolytic therapy, have used radio immunoassays or electrophoresis for measuring CKMB level, which requires long assay times or are not analytically sensitive[7,10,11,12].

Other studies have examined the time to peak (6-12 hours after onset of symptoms) of serum CKMB. Some of these have not included acute angiography to verify the reperfusion status. These limitations do not allow for early, accurate determination of reperfusion status. In present study 95% of patients having patent infarct-related artery proven by angiography had peak CKMB activity within 12 hours of start of thrombolytic therapy. This gives high degree of sensitivity (95%) for prediction of reperfusion. However due to logistic problem angiography was not performed immediately after therapy. A disadvantage of CKMB peak as a reperfusion marker is, of course, the fact that the test results are only available hours after completion of myocardial necrosis. However, it has been demonstrated that the time to peak CKMB activity can be substituted by the rapidity of the initial release of this enzyme within the first 90-120 minutes of thrombolytic therapy[7,10].

The rapid analysis of myoglobin and Troponin-T may offer additional advantages because of earlier initial increase in serum concentration[13].

The value of reperfusion arrhythmia as a marker of reperfusion remained a matter of debate. The major findings of this study are: (i) Reperfusion arrhythmias are not frequently seen during thrombolysis for AMI and occurred only in 31% of patients who had restoration of antegrade flow; (ii) the arrhythmias most frequently seen were accelerated idioventricular rhythm in cases of anterior wall AMI and sinus bradycardia when vessel supplying the inferoposterior

left ventricle were recanalized; and (iii) specific therapy for the arrhythmias was usually not required.

Conclusion

Non-invasive methods of monitoring reperfusion of infarct-related artery can be used to identify the majority of patients with inadequate perfusion. By using such approach it has been possible for early triage of such patients and consideration for rescue angioplasty.

The study revealed that percent (%) ST change > 50 resolutions at 90 minutes of start of thrombolytic therapy provides a method that is both specific and sensitive. CKMB peak within 12 hours gives high degree of sensitivity but low specificity. Reperfusion arrhythmias turned out to be poor indicator of reperfusion having low sensitivity. So study concludes

TABLE - 7

Sensitivity, Specificity and Positive and Negative Predictive Value of Non-Invasive Markers with Respect to a Patent Infarct Related Artery

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Single Marker				
ST elevation reduction ≥ 50%	85	76	82	79
CKMB peak ≤ 12 hours	95	48	71	87
Reperfusion Arrhythmia	31	86	75	48
Combined Analysis				
ST segment elevation reduction + CKMB peak + reperfusion arrhythmia	70	70	76	64
ST segment elevation reduction + CKMB peak	89	62	76	82

Key: PPV = Positive predictive value
NPV = Negative predictive value

that ST segment settling and CKMB peak can be utilized for prediction of reperfusion in our local population.

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