ST-SEGMENT RESOLUTION: A CRITERION OF SUCCESSFUL THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background: Thrombosis of the coronary artery is the principal cause of myocardial infarction in the territory of the affected vessel. To limit the size of infract area and for the salvage of the jeopardized myocardium, restoration of patency of infarct related coronary artery is very important to reduce morbidity and mortality in these patients.[1,2] The physician's ability to predict patency of the infarct related artery from clinical variables however is disappointing. The role of ST-segment resolution during an ST segment infarction has over the years, grown into not only an alternative way of approximating risk and chances of reperfusion in the absence of a coronary angiogram, but also a method challenging the traditional "gold standard" for predicting risk and reperfusion at the myocardial level. Thus, ST-segment resolution at 90 minutes is an excellent marker of successful myocardial reperfusion[1] and a strong predictor of survival and preservation of left ventricular function.[3-5]

Aims & Objectives: We studied the relation between ST-segment resolution and various outcomes in cases of acute myocardial infarction at our institute.Our aim was to study ST-segment resolution as a marker and a simple bedside tool for predicting of successful myocardial reperfusion, 90 minutes after thrombolysis in STEMI (ST elevation myocardial infarction).We also studied and attempted to correlate ST-segment resolution at 90 minutes after thrombolysis as a predictor of recovery, in-hospital adverse events, morbidity and mortality in STEMI.

Methods: The present study was conducted on 50 patients who had received thrombolytic therapy with streptokinase for ST Elevation AMI, in our ICCU. Detailed clinical history with specific emphasis on presenting complaint and associated coronary risk factors and management done were captured.

Results: The study corroborates the evidence that the recanalization and the patency of the IRA (Infarct Related Artery) remained higher in the patients with complete resolution of ST-segment at 90 minutes group, than the patients with partial resolution and the no resolution groups.

Conclusions: ST-segment resolution can be used as a simple non-invasive tool for the prediction of the patency of the IRA after thrombolysis.

Keywords: St-segment, resolution, Acute Myocardial Infarction, thrombolysis.

INTRODUCTION

India is experiencing an alarming increase in heart diseases. Cardiovascular diseases accounted for 32% of all deaths in 2000 and the WHO estimated that 60% of the world's cardiac patients will be Indian by 2010. Thrombosis of the coronary artery is the principal cause of myocardial infarction in the territory of the affected vessel. To limit the size of infract area and for the salvage of the jeopardized myocardium, restoration of patency of infarct related coronary artery is very important to reduce morbidity and mortality in these patients.[2,6] The importance of early reperfusion after acute myocardial infarction (MI) has been clearly

demonstrated.[2] Recanalization of infarct related vessel is achieved by either pharmacological agents or by surgical interventions like PTCA or CABG. As surgical intervention is very costly and very limited in availability, pharmacological recanalization becomes more practical in this country.

The physician's ability to predict patency of the infarct related artery from clinical variables however is disappointing.[1,7] There are certain non-invasive bedside markers which help us in knowing the patency of infarct related coronary artery like, significant reduction in chest pain, early peaking of serum Creatine Kinase (CPK-MB) level, reperfusion arrhythmias, > 70% reduction in ST segment elevation. Though coronary angiography is the preferred way to know the patency of infarct related vessels[7], these non-invasive bed side markers are not yet to be overlooked specially in our country and set-up.

Even in developed countries (like USA) this simple bedside tool of ST-segment resolution tends to be neglected as an indicator of prognosis of guide to further management. Decision on matters such as length of hospital stay and selection for angiography or treadmill investigation are determined mainly by in-hospital clinical events or age.[8] Currently in our country, most districts general hospitals lack rapid access to angioplasty and owing to financial constraints, must rely solely on thrombolytic therapy in the first instance.

Thrombolytic therapy for acute myocardial infarction reduces case fatality and improves clinical outcomes.[2,6] The role of ST-segment resolution during an ST segment infarction has over the years, grown into not only an alternative way of approximating risk and chances of reperfusion in the absence of a coronary angiogram, but also a method challenging the traditional "gold standard" for predicting risk and reperfusion at the myocardial level. Thus, ST-segment resolution at 90 minutes is an excellent marker of successful myocardial reperfusion[1] and a strong predictor of survival and preservation of left ventricular function.[3-5]

In this observational study, we investigated the short term and long term implications of ST-segment resolution and non-resolution after thrombolytic therapy. This study is done on one of the markers, i.e. "ST-Segment resolution as a criterion of successful thrombolysis in patients of Acute Myocardial Infarction."

MATERIAL AND METHODS

The present study was conducted during March 2008 to October 2009 on 50 patients who had received thrombolytic therapy with streptokinase for ST Elevation AMI, in our ICCU. Detailed clinical history with specific emphasis on presenting complaint and associated coronary risk factors sought. After thorough clinical examination, ECG was taken and repeated serially. Creatine Kinase (CPK-MB) and Troponin-I were measured immediately at admission, along with routine investigations like complete blood count, renal function test, lipid profile, blood sugar, liver function test and chest x-ray.

Inclusion Criteria

(1) Symptoms of Acute Myocardial Infarction. Chest pain at rest, lasting >20 minutes to <6 hours at hospital admission.

(2) ST Elevation >0.1 my in two or more limb leads or >0.2 mV in two or more contiguous precordial leads.

(3) Age >18 years.

(4) Patients of AMI, where thrombolysis was indicated.

(5) Patients of AMI who were eligible and ready to undergo CAG thereafter.

(6) Electrocardiography criteria.

Exclusion Criteria

(1) Patients with STEMI having chest pain for >6 hours at admission to hospital.

(2) Patients who had contraindications to thrombolytic therapy.

(3) Patients who had any known history of stroke / TIA (transient ischemic attack) and those who had received any Gp2bIIIa inhibitors within preceding 12 hours were excluded.

(4) Patients who died within 180 minutes of randomization.

Electrocardiography Criteria

A 12 lead ECG was obtained from all patients of AMI. A baseline ECG was defined as having been obtained no more than 2 hours before or 8 minutes after the initiation of thrombolytic therapy. Follow up EGGs were obtained from all patients at 90 minutes after the thrombolytic therapy began. Other ECGswere also obtained between 60 and 120 minutes after the initiation of therapy.

The amount of ST-segment elevation to the nearest 0.1 mV was measured at the J point. The sum of all ST-segment elevation included all leads with >0.1 mV of elevation. The sum of "Anterior ST-segment elevation" included leads I, aVL, V1-V6. The value for inferior ST-segment elevation included leads II, III, aVF.All measurements were made at a core electrocardiographic laboratory that was blinded to both treatment assignment and patient outcomes. The prognostic importance of ST-segment change was made on the basis of 3 categories of ST-segment resolution.

Complete resolution of ST segment was defined as >70% resolution of the sum of ST-segment elevation. Partial resolution was defined as>30% but <70% resolution. No resolution was expressed as <30% resolution of the sum of the ST-segment elevation. A random audit of 5%of all ECGs was performed to verify the accuracy of data.2D Echocardiograph was done in all the patients, 24 hours after thrombolysis. Coronary Angiography (CAG) and revascularization procedures were also done as standard care from 24 hours up to 5 days after thrombolysis, considering the financial constraints of the patient, wherever applicable.Appropriate statistical tools were applied to interpret test of significance and comparison of two groups.

RESULTS

The study was conducted on 50 patients admitted in the ICCU.Among 50 patients who were randomly selected for the study, 43 (86%) were males and 7 (14%) females.Among the 50 patients who were randomly selected, the age varied from 40 years to 74 years and the mean age of the patients was 58 years. Age happened to be the single most important non-modifiable risk factor. Withincrease in the age, increased risk of coronary artery disease, morbidity, mortality and the degree of non-resolution of ST segment at 90 minutes after thrombolysis was observed.

Table-1: Distribution of age among ST-Segment resolution group

Age (Years)	Complete Resolution (>70%, n=23)	Partial Resolution (>30% to <70%, n=14)	No Resolution (<30%, n=13)
<40	4.34% (1/23)	7.14(1/14)	0%
41-50	47.82% (11/23)	14.26 (2/14)	30.76(4/13)
51-60	26.08 (6/23)	50.0 (7/14)	30.76(4/13)
61-70	21.73(5/23)	28.57 (4/14)	23.07(3/13)
>70	0%	0%	15.38(2/13)

The patients in the younger age group (41-50 years) had higher chances of complete resolution of ST-segment at 90 minutes, while those in the older age group (>51 years) had higher chances of no resolution or partial resolution as indicated in the Table-1.The occurrence of in-hospital adverse events, morbidity and mortality were more in the older age group. One of the patients who expired

in the study group belonged to >70 years age group.

The incidence of dyslipidemia was 92%. Tobacco smoking, Type-II DM, HT, Obesity and past history of IHD was present in 56%, 34%, 30%,22% and 12% respectively.Of the 50 patients who were randomly selected for the study, 29 patients (58%) had anterior wall ST Elevation Myocardial Infarction (STEMI) and 21 patients (42%) had inferior wall STEMI, among them 84% of patients (n=42) presented in Killip Grade I & II and 16% (n=8) of patients in Killip Grade III & IV at the time of admission.

Within the study (n=50), 46% of the patients had complete resolution (>70%) of ST-segment at 90 minutes as compared to 28% of partial resolution (<30% to <70%) and 26% had no resolution (<30%).The majority of the patients in the complete resolution at 90 minutes group had inferior wall infarction (60.8%) as against anterior wall infarct (39.2%).Thus the patients with anterior wall infarction were more likely to have no resolution or partial resolution at 90 minutes. These findings are in concordance with the GUSTO-III trial study data.[9]

There was no difference in the distribution of markers of previous coronary artery disease such as prior M.I., angina, CHF, CABG, HTN, DM II, smoking at presentation among the various groups of ST segment resolution.Thus, patients with anterior wall infarction were more likely to have no or partial ST segment resolution at 90 minutes after thrombolysis than were the patients with inferior wall infarction (P=0.001).The occurrence rates of CHF, cardiogenic shock and in-hospital mortality were higher in the patients with no resolution and partial ST segment resolution

groups when compared to complete ST segment resolution group at 90 minutes, as shown in Table-2. The relationship between the five most predictive variables from the GUSTO-I mortality model[10] and categorical ST-segment resolution at 90 minutes revealed several groups to be at high risk for hospital adverse events and morbidity as shown in Table-2.The single patient, who expired in the study on day two after thrombolysis, belonged to the no-resolution group and had associated cardiogenic shock as acomplication.The patients in the complete ST resolution group had lesser adverse events and were discharged earlier from the hospital as compared to their counterparts in the partial and no resolution groups.

The patients in the complete ST resolution group had lesser adverse events and were discharged earlier from the hospital as compared to their counterparts in the partial and no resolution groups. Among the patients with no ST-segment resolution at 90 minutes, who were at high risk for hospital adverse events and morbidity included the following:

(1) Patients aged >70 years (23.08%) in the study group

(2) Those with Killips Class >I (100%).

(3) Those with anterior all infarctions (76.9%) than inferior wall infarction (23.1%) in the study group.

Patients with no resolution at 90 minutes who presented with tachycardia (HR>110 beats/min) or systolic hypotension (SBP<90 mmHg) had a high morbidity and significant mortality rate (7.69%) among the study group.Patients aged >70 years, or with Killip classification >I, who had partial resolution of ST-segment elevation were also at an increased risk for morbidity and mortality.

Table: 2 Characteristics of cases resolution of the ST-segment elevation (Sum of) at 90min

(%)	No Resolution	Partial Resolution	Complete

	(<30%)	(>30% to <70%)	Resolution (>70%)
Resolution at 90 minutes	n=13	n=14	n=23
Age (years)	62	58	58
Female (%)	4	4	6
HTN (%)	46.15	42.85	34.13
Diabetes (%)	38.46	28.57	34.13
Current Smoker (%)	53.84	42.85	65.20%
Past History (%)			
Ml	7.6	7.6	7.6
Angina	15.38	15.38	15.38
CHF	0	0	0
PTCA	0	0	0
CABG	0	0	0
Systolic BP* (mmHg)	128(120,180)	130(120,180)	134(120,180)
H.R. (beats/min)*	92/min	84/min	88/min
M.I.Location (%)			
Anterior	76.9	64.2	39.2
Inferior	23.1	35.8	60.8
Time to treatment (Hrs)*	3.1	3	3.1
Age			
15-70	76.92	92.86	100
>70	23.08(3/13)	7.14	0
KillipClass(%)			
I	0	28.57	78.23
>I	100	71.43	21.73
Infarct Location (%)			
Anterior	76.9	64.2	39.2
Inferior	23.1	35.8	60.8
Complications			
CHF	53.84	21.42	4.34
Cardiogenic shock	15.38	7.14	0
Angioplasty	84.61	85.71	69.56
CABG	15.38	7.14	8.69
In-Hospital mortality	7.6	0	0
Average length of hospital stay (Days)	10	7	5
Recanalization of IRA at CAG	0	7.14	21.73
Ejection Fraction (EF in %)			
< 40 (Poor)	4.35 (1/23)	42.86 (6/14)	92.3(12/13)
> 40 (Fair to Good)	95.65 (22/23)	57.14(8/14)	7.7(1/13)

Higher proportion of the patients who had complete resolution of ST-segment had good ejection fraction of >40% (95.65% patients) as compared to partial (57.14%) and no resolution

(7.7%) groups. Regional wall motion abnormality was found in majority of the patients and did not show much of inclination towards any particular group.Left ventricular aneurysm was found as a complication in one patient with anterior wall M.I. (No-resolution ST segment) and this patient died on day two after thrombolysis.

The characteristics of IRA (Infarct Related Artery) from CAG in terms of patency, percentage of occlusion, recanalization and number of vessels involved in patients with complete, partial or no resolution of ST segment at 90 minutes are shown in Table-2. This study shows that the chances of

recanalization and the amount of patency of the IRA tends to remain higher in patients with complete resolution of ST segment at 90 minutes after thrombolysis then compared to partial or no resolution.

The recanalization of the IRA was seen in 21.73% of the patients with complete resolution as compared to 7.14% in partial resolution group. No recanalization was found in patients with no resolution. 84.61% of the patients in no Resolution group had 91-100% occlusion of IRA as compared to 50% and 39.13% of the patients with partial or complete resolution group respectively.
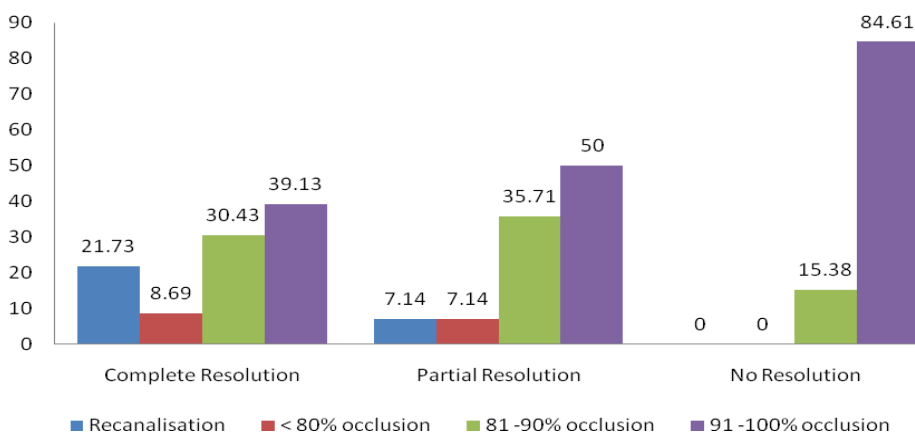

Figure: 1 Characters of IRA in different ST-resolution groups

There was no significant variation in the distribution of PTCA or CABG characteristics within the ST-segment resolution groups at 90 minutes. But the recanalization of the IRA and lesser significant occlusion (<80% occlusion of IRA) were seen more in the complete ST-segment resolution group at 90 minutes after thrombolysis. The study shows that the patients in the complete ST-segment resolution at 90 minutes group were discharged earlier from the hospital at an average of 5 days after admission as compared to partial resolution (Average 7 days) and no resolution groups (Average 10 days). This can be explained by the fact that, the incidence of complications and morbidity were more in the no resolution and

partial resolution groups and hence took longtime to recovery.

DISCUSSION
Previous Studies of ST-Segment Resolution
Saran *et al*[11] have shown that >25% ST-segment resolution in the leadwith the greatest elevation at 3 hours is predictive of both coronary arterypatency and improved left ventricular function. Barbashet al[4] extended thisconcept to include the sum of ST-segment elevation. The resolution of thesum of ST-segment elevation at 1 hour correlated with patency of the infarct-related artery at 72 hours, smaller enzymatic infarcts, better left ventricularfunction, and lower mortality.[4] Investigators from the Gruppo Italiano

per lo Studio della Sopravvivenzanell' Infartomiocardo (GISSI-2) study[12] showedthat normalization of ST-segment resolution at 4 hours was similarly predictiveof patient outcome. In a study by Matetzky *et al*[13], resolution of ST-segmentelevation in patients with acute Ml with early peaking creatine kinase afterthrombolytic therapy helped differentiate between those with and without adequate myocardial perfusion. Dissmann[14] was the first to propose 3categories for resolution of ST-segment elevation on the basis of ≥70% cut off point identified by his group and combined with the cutoff point fromSaran's group.[11] These investigators demonstrated a relationship betweenincreasing ST resolution, smaller infarct size, and better left ventricularfunction at follow-up.[14] Schroder then verified these cut-out points in theIntravenous Streptokinase in Acute Myocardial Infarction (ISAM) trial[3] andlater validated them prospectively in the International Joint Efficacy Comparison of Thromboses (INJECT) trial.[15] Schroder reported that by use of the 3 categories of Dissmann, ST-segment resolution at 180 minutes is predictive of 35-day morbidity and mortality. Finally, investigators from the Hirudin for the Improvement of Thrombolysis (HIT-4) trial reported that resolution of the sum of ST-segment elevation was an important prognostic indicator for 30-day mortality both at 90 and 180 minutes, suggesting the importance of this variable at the 90-minute time point.[16,17] Recently, the TIMI group has shown similar data in a smaller angiographic trial.[17]

Independent Predictors of Mortality

This study report is in concordance with - A substudy of the GUSTO-III trial - predicting outcome after thrombolysis in acute myocardial infarction according to ST segment resolution at 90 minutes,[9] one of the largest prospective analyses of the ST-segment resolution variable. It reveals how simple, noninvasive, and easily obtained electrocardiographic data can risk-stratify patients as early as 90 minutes after the initiation

of thrombolysis. The resolution of the sum of ST-segment elevation at 90 minutes has significant prognostic importance.[9] Certain subgroups were found to be at high risk of mortality, including patients who had partial or no resolution of the sum of elevated ST segments at 90 minutes and were aged >70 years, and those with any signs of heart failure (Killip class>I). In addition, patients in the partial and no resolution groups had significantly higher rates of in-hospital CHF and cardiogenic shock. To our knowledge, this has been previously demonstrated in GUSTO-III Trial.[9] The importance of ST-segment monitoring for early identification and triage of patients with acute coronary syndromes to possible rescue PTCA has been recently shown. The benefit of the invasive approach for early identification of patients in cardiogenic shock was also recently underscored by the 6-month results of the intervention trial, should we emergently revascularize **O**ccluded **C**oronaries for cardiogenic shock? (SHOCK).[18]

Sum of Categories of ST-Segment Resolution

Dissmann's original categories of ST-segment resolution were partly basedon the observation that infarct size and worsening mortality were associated with <70% ST-segment resolution.[14] Additionally, Saranhad reported worse left ventricular function with <25% resolution.[11] We had the opportunity to validate this cut-off point at 90 minutes after thrombolysis. For predicting the outcome ofmyocardialreperfusion, preservation of left ventricular function and in-hospital morbidity and mortality on the basis of individual deciles of ST-segment resolution, a relatively consistent relation between ST segment resolution at 90 minutes and in-hospital adverse events has been shown in our study. As the degree of resolution increases, the mortality and morbidity decreases. However, the most reliable measure appears to be ≥70% sum of ST segment resolution, as those patients had consistently low in-hospital adverse events, lesser length of hospital stay, good preservation of left

ventricular function and myocardial reperfusion, by the use of 90 minute time point. The categories used by Schroder[3,15], therefore, seem reasonable and apply to the earlier time point as well.

Epicardial and Myocardial Reperfusion

The relationship between the resolution of ST-segment elevation andoutcome appears to be independent of epicardial or infarct-related artery patency. In astudyof117 patients who underwent successful direct angioplasty, subjects were categorized into 2 groups: those with <50%reduction in ST-segment elevation and those with ≤50% reduction in thelead with the greatest ST-segment elevation. At 1-month follow-up, patientswith ST resolution had betterrecovery of left ventricular function, as well ashigher ejection fractions. Multivariate analysis revealed ST-segment reductionto be the only predictor of functional recovery. In a similar study of 403patients who underwent primary angioplasty, patients with patent infarct-related artery and resolution of ST-segment elevation had smaller infarcts,better follow-up left ventricular function, and lower mortality. Other studieshave shown that poor myocardial perfusion predicts worse morbidity andmortality, even when reperfusion methods are considered successful. Thesestudies suggest that myocardial perfusion is strongly correlated with outcomeand that it may be better predicted by ST-segment resolution than by infarct-related artery patency.

ST-segment resolution on a standard 12-lead ECG, at 90 minutes after the thrombolytic therapy, is an independent predictor of morbidity and mortality. This marker is inexpensive, easy to perform, and available at the patient's bedside. When used 90 minutes after the initiation of therapy, lack of ST-segment resolution aids in identifying high risk patients who may benefit from additional therapies like rescue PTCA. As studies in these area continues, we may find optimum monitoring time to be <90 minutes, as preliminary reliability of results obtained as early as 60 minutes after administration of thrombolytic therapy.[18] Weather

an earlier time point is an independent predictor of mortality remains to be determined. Further studies should determine whether outcome in patients within patients without 90 minutes ST-segment resolution could be improved by rescue PTCA. However, other randomized trials have suggested a benefit with revascularization procedures in high risk patients with acute MI.

CONCLUSIONS

The ST segment resolution at 90 minutes after thrombolysis is a significant marker of preservation of left ventricular function as evidenced in the study. The patients in the complete resolution group had better ejection fraction as compared to the partial resolution and the no resolution groups. The study corroborates the evidence that the recanalization and the patency of the IRA (Infarct Related Artery) remained higher in the patients with complete resolution of ST-segment at 90 minutes group, than the patients with partial resolution and the no resolution groups.

Thus, ST segment resolution can be used as a simple non-invasive tool for the prediction of thepatency of the IRA after thrombolysis.

ACKNOWLEDGEMENTS

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