To Study the Resolution of Electrocardiogram Changes As A Non-Invasive Predictor of Clinical Outcome And Prognosis in Post Thrombolytic Patients with Acute Myocardial Infarction in A Tertiary Care Centre of North India

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Abstract: *The aim of the study was to determine the in-hospital prognosis of patients with and without ST segment resolution in the electrocardiogram who received thrombolytic therapy for acute myocardial infarction. This was a 1 year prospective study and all patients of acute myocardial infarction who received thrombolytic therapy were included in the study. Clinical features, resolution of ECG changes at 60 minutes, 120 minutes and 180 minutes was recorded and the complications of the patients were studied and the data was analyzed by the appropriate statistical methods.*
Keywords: *Acute myocardial infarction, clinical outcome, prognosis, resolution, ST segment changes*

I. INTRODUCTION

Ischemic heart disease in India has been on the rise since the past few decades. About 40 million people suffer from Heart disease in the Indian subcontinent (1).The factors which are responsible for the increased incidence being smoking, mounting stressful jobs, lifestyles, high fat, high cholesterol diet, all of them contribute to the increase in the incidence of ischemic heart disease (2).Myocardial infarction is a potential sequel to angina. The immediate objective is to produce a rapid and haemodynamicaly effective recanalization of the occluded artery and the ultimate goal of therapy is in achieving myocardial viability. Approximately 50% of deaths associated with acute myocardial infarction occur within one hour of the event and are most commonly attributableto arrhythmias, (American Heart Association 1996) which are most often ventricular arrhythmias(3).

The advent of coronary thrombolysis after 1980 as primary therapy for acute myocardial infarction then revolutionized management of patients presenting with acute myocardial infarction to the hospital. The aim of thrombolysis in acute myocardial infarction is early and complete myocardial reperfusion.Reperfusion is achieved in patients receiving thrombolytic therapy for myocardial infarction by either opening up of the occluded vessel or by the formation of effective collaterals to bye pass the occlusion.Yet reperfusion fails in a significant proportion of patients (4).Incomplete or delayed reperfusion is associated with an increased risk of death and left ventricular dysfunction. The gold standard for the diagnosis of failed reperfusion is a combination of coronary angiography and myocardial contrast imaging but this is impractical for routine clinical use. Hence there was a search for non-invasive markers to assess reperfusion. Resolution of chest pain, EKG changes and biochemical markers have been studied to assess reperfusion non-invasively (5) Biochemical tests have also been considered to assess failed reperfusion. Inspite of the high sensitivities and specificities described, in view of the need for frequent blood sampling and specialized laboratory facilities, the assessment of reperfusion by estimation of creatine – kinase isoenzymes, troponin T and myoglobin have not been routinely used for prospective analysis of reperfusion.(6)

The post thrombolytic electrocardiogram has shown promise as a non-invasive marker of reperfusion. Previous studies have shown an association between early resolution of ST segment elevation after thrombolysis and improved coronary patency and clinical outcome (7).There have not been many Indian studies which were

done to compare prospectively the prognostic accuracy of a 50% decrease on the ST segment elevation in standard 12 lead EKG's done in the early hours (namely 1st hour, 2nd hour and 3rd hour) following thrombolytic therapy for acute myocardial infarction. Hence this study was done to determine the in- hospital prognosis of patients with and without ST resolution in terms of mortality and let ventricular ejection fraction and complications such as arrhythmias and left ventricular failure.

II.   AIM OF THE STUDY

To determine the in-hospital prognosis of patients with and without ST segment resolution following thrombolysis

III.   MATERIALS AND METHODS

This prospective study included all patients of acute myocardial infraction who received thrombolysis admitted to ICCU of Christian Medical College and Hospital, Ludhiana from August 1, 1998 to July 31st 1999. Myocardial infarction was diagnosed by WHO criteria. A detailed history, clinical and laboratory investigation was done at the time of admission according to the protocol. All patients with Acutemyocardial Infarction (AMI) presenting with chest pain within 12 hours of onset received Intravenous streptokinase infusion 1.5 million units in 100 ml normal saline over one hour.

IV.   METHODS

A baseline 12 – lead ECG was recorded immediately before initiation of thrombolysis and at 60minutes, 120 minutes and 180 minutes thereafter. The ST segment was measured by caliper at 80 milli seconds beyond the J point. The lead with maximum ST elevation was determined from the baseline ECG and used for subsequent measurements. ST segment deflection at 60 minutes, 120 minutes and 180 minutes was compared with the baseline ECG. Sum ST elevation was also calculated by adding together the ST elevation for the leads other than aVR. A 50% reduction in ST segment elevation in the chosen lead or in sum ST elevation compared with baseline was the criteria for reperfusion. Study patients were then divided into two groups :-
1. Patients with ST resolution.
2. Patients without ST resolution.

Exclusive criteria:
1.   Patients with old infarctions.
2.   Technically poor quality ECG's.
3.   Patients with bundle branch blocks.
4.   Patients who received thrombolysis outside the hospital.
5.   Patients who died before the end of 180 minutes following thrombolytic therapy

Statistical methods:
Student – T test and Chi square test was used for the analysis of the data as applicable.

V.   RESULTS

A total of 99 patients were studied and various haematological and biochemical tests were performed in each group.Outcome was studied in terms of post – infarction arrhythmias, LVF and mortality for the time period till discharge and complications were noted.

Table – 1 (A)
Age of Males in 2 study Groups

Age	ST Resolution	No ST Resolution
Range (yrs)	22 – 75	35 – 67
Mean ± SD (yrs)	54.82 ± 12.82	52.82 ± 9.68

The mean age of the male patients in Group 1 was 54.82 ± 12.82. The mean age of the male patients in Group 2 was 52.82 ± 9.68.

Table – 1 (B)
Age of Females in 2 study Groups

Age	ST Resolution	No ST Resolution
Range (yrs)	40 – 76	76 – 79
Mean ± SD (yrs)	58.54 ± 9.28	79 ± 0.0

The mean age of the female patients in Group 1 was 58.54 ± 9.28 and in Group 2 was 79 ± 0.0.

Table – 2
Age and Sex Distribution

Age group	Male	Female	Total
< 50 years	25 (32.9%)	4 (17.4%)	29 (29.29%)
> 50 years	51 (67.10%)	19 (82.6%)	70 (70.71%)
Total	76 (76.8%)	23 (23.2%)	99

Among the males 25 (32.9%) of patients were found to be less than 50 years and 51 (67.10%) of them were found to be above 50 years.Among females 4 (17.4%) of patients were less then 50 years and 19 (82.6%) of them were found to be above 50 years.

Table – 2
Symptoms at Presentation

Symptoms	ST Resolution	No ST Resolution
Chest pain	69 (93.2%)	22 (88%)
Sweating	51 (68.9%)	14 (56%)
Shortness of breath	14 (18.9%)	10 (40%)
Giddiness	7 (9.5%)	5 (20%)
Orthopnea	3 (4.1%)	4 (16%)
Palpitation	31 (41.9%)	5 (20%)
Shoulder pain	36 (48.7%)	7 (28%)

In the Group 1 with ST resolution 69 (93.2%) had chest pain whereas in the Group 2, 22 (88%) had chest pain which was not statistically significant.51 (68.9%) of the patients with ST resolution had sweating as the presenting symptom, whereas in patients with no ST resolution 14 (56%) had sweating as the presenting symptom which was not statistically significant.

Table – 3
Status of ST at Different time

Time	ST Resolution	No ST Resolution
1st Hour	75 (75.8%)	24 (24.2%)
2nd Hour	82 (82.8%)	17 (17.2%)
3rd Hour	82 (82.8%)	17 (17.2%)

From the present study it is seen that 75 (75.8%) achieved ST reduction in the first hour and 24 (24.2%) did not achieve 50% ST reduction in the first hour.At the 2nd hour, 82 patients (82.8%) achieved ST reduction as against 17 (17.2%) in the second hour.In the third hour 82 (82.8%) patients achieved ST segment reduction as against 17 (17.2%) in the third hour.

Table – 4
Window Period and Associated Mortality

Window Period	ST Resolution	No ST Resolution	Total
0 – 4 hours	39 (52.7%)	11 (44%)	50 (50.5%)
Mortality	2 (5.1%)	0	
5 – 8 hours	26 (35.1%)	3 (12%)	29 (29.3%)
Mortality	1 (3-8%)	1 (33.3%)	
9 – 12 hours	9 (12.2%)	11 (44%)	20 (20.2%)
Mortality	0	0	

50 (50.5%) patients presenting within 4 hours of the onset of chest pain received streptokinase and 39 (52.7%) achieved ST resolution against 11 (44%) who did not achieve ST resolution. In this window period there were 2 (5.1%) mortalities. 29 (29.3%) patients presented at 5 – 8 hours of the onset of chest pain and 26 (35.1%) of them achieved ST resolution against 3 (12%) who did not achieve ST resolution. In the 5 – 8 hours window period there were 2 mortalities (37.1%). 20 (20.2%) patients presented between 9 – 12 hours of the onset of chest pain. 9 (12.2%) of them achieved ST resolution against 11 (44%) patients who did not achieve ST resolution. In the window period 9 – 12 hours window period there were 2 mortalities (37.1%).

Table – 5
Blood Pressure

Blood Pressure	ST Resolution	No ST Resolution
Systolic Range	80 – 180	100 – 210
Mean ± SD	128.5 ± 21.23	138 ± 24.49
Diastolic Range	50 – 190	70 – 110
Mean ± SD	89.5 ± 21.52	92.4 ± 13.3

The mean systolic and diastolic blood pressure in Group 1 with ST resolution was 128.5 ± 21.3 and 89.5 ± 21.52.The mean systolic and diastolic blood pressure in Group 2 with no ST resolution was 138.5 ± 24.9 and 92.4 ± 13.3.

Table – 6
Laboratory Tests

	ST Resolution	No ST Resolution
Haemoglobin Range	8 – 15	7 – 17
Mean ± SD	14 ± 4.73	13.72 ± 2.3
TLC Range	4400 – 25000	6000 – 23000
Mean ± SD	11494 ± 4538	10468 ± 3923
Platelets Range	1 – 8 (Lac)	1 – 4 (Lac)
Mean ± SD	2.135 ± 0.896 (Lac)	2.08 ± 0.64 (Lac)
FBS Range	82 – 360	72 – 304
Mean ± SD	146.43 ± 62.15	129.92 ± 59.99
Potassium Range	3 – 5	3 – 6
Mean ± SD	4.23 ± 0.53	4.24 ± 0.59
Cholesterol Range	81 – 318	123 – 252
Mean ± SD	197.99 ± 52.49	186 ± 37.25
Triglycerides Range	49 – 817	54 – 317
Mean ± SD	171.17 ± 136.38	141.16 ± 68.23

Mean haemoglobin was 14 ± 4.73 in the group 1 with ST resolution and 13.72 ± 2.3 in group 2 without ST resolution.Mean leucocyte count in group 1 with ST resolution was 11,494 ± 4538 and 10,468 ± 3923 in group 2 with no ST resolution.Mean platelet count in group 1 with ST resolution was 2.135 ± 0.89 and 2.08 ± 0.64 in group 2 with no ST resolution.Mean fasting blood sugar (FBS) in group 1 with ST resolution was 146.43 ± 62.15 and 129.92 ± 59.99 in group 2 with no ST resolution.The difference in the 2 groups for any of the tests was statistically not significant.

Table – 7
Cardiac Enzymes

Cardiac Enzymes	ST Resolution	No ST Resolution
CPK1 Range	21 – 3295	440 – 4070
Mean ± SD	494.93 ± 673.95	623.24 ± 905.9
CPK2 Range	32 – 9975	51 – 8925
Mean ± SD	1908.56 ± 1868	1575.56 ± 1761.72
LDH1 Range	50 – 1505	250 – 1650
Mean ± SD	460.1 ± 252.5	616.6 ± 395.1
LDH2 Range	125 – 3140	110 – 2545
Mean ± SD	1135 ± 712	1218.6 ± 725.7
AST1 Range	11 – 3970	17 – 407
Mean ± SD	120.8 ± 457.56	106.4 ± 105
AST2 Range	19 – 3675	15 – 687
Mean ± SD	341 ± 459.4	253.1 ± 178.4

A lower CPK1 mean 494.93 was observed in group 1 patients as compared to group 2 patients where it was 623.24. A higher CPK2 mean 1908.56 was observed in group 1 patients as compared to group 2 in which the mean was 1575.56. A lower LDH1 mean 460.1 was observed in group 1 as compared to 616.6 in group 2. In group 1 LDH2 mean was 1135 as compared to 1218.6 in group 2. The difference in the mean value of any of the cardiac enzymes was statistically not significant.

Table – 8 Status of ST Associated LVEF at Different Hours

Status of ST	LVEF < 40%	LVEF > 40%
ST Resolution		
1st hour	43 (57.3%)	32 (42.7%)
2nd hour	47 (57.3%)	35 (42.7%)
3rd hour	46 (56.1%)	36 (43.9%)
No ST Resolution		
1st hour	17 (70.8%)	7 (29.2%)
2nd hour	30 (76.5%)	4 (23.5%)
3rd hour	14 (82.4%)	3 (17.6%)

Among the persons who achieved ST resolution, 32 (42.7%) patients had LVEF > 40% in the first hour, 35 (42.7%) in the second hour and 36 (43.9%) in the third hour had LVEF > 40%.Among the persons who

did not achieve ST resolution 17 (70.8%) patients in the first hour, 30 (76.5%) patients in the second hour and 14 (82.4%) patients in the third hour had LVEF < 40%.

Table – 9 Overall Mortality

Condition on Discharge	ST Resolution	No ST Resolution	Total
Alive	71 (95.9%)	24 (96%)	95 (96%)
Dead	3 (4.1%)	1 (4%)	4 (4%)
Total	74 (74.7%)	25 (25.3%)	99

Among the Group 1 patient with ST resolution there were 3 (4.1%) deaths and among Group 2 patient with No ST resolution there was 1 (4%) death.The difference between the 2 groups in relation to mortality was not statistically significant (p > 0.05).

VI. DISCUSSION

Coronary artery disease has shown a gradual rise in India. The study was undertaken to find out the predictive accuracy of early EKG's on patients who receive streptokinase as treatment for acute myocardial infarction. All patients received heparin, Aspirin, β – blockers, calcium channel blockers and nitrates as applicable. Patients were monitored daily during their hospital stay till discharge and complications arising were noted.The benefits of thrombolytic therapy are maximum if instituted within a few hours of the onset of myocardial infarction and become negligible after 12 hours of onset of myocardial infarction in clinical studies. Andersen et al, 1984 showed that with thrombolytic therapy death within the first few weeks of myocardial infarction declined from 10 – 15% to 5 – 10% with better recovery of left ventricular function, fewer arrhythmias and better long term survival.(8) The mortality reduction was highly significant among patients presenting within 3 hours of symptom onset with 26% proportional reduction and among those presenting 4 – 6 hours of onset 18% proportional reduction (Fibrinolytic Therapy Trialists (FTT) collaboration group, 1994).(9) Time to thrombolysis influenced the proportion of patients achieving a 50% decreased in ST segment elevation at each time point. Purcell et al 1997 in a study on 190 patients observed that the longer the window period the lesser the number who achieved ST resolution and the shorter the window the higher was the ST segment resolution.(10) In the present study within the window period 0 – 4 hours, there was a larger number and percentage of patients compared to the figures in the window periods 5 – 9 hours and 9 – 12 hours. There are also a greater proportion of patients achieving STsegment resolution the earlier they received thrombolytic therapy. In view of the small number of overall mortality, the difference in the two groups with respect to mortality at each of the window periods cannot be compared.

It is seen from the observation that there is an increasing knowledge and awareness of the benefit of early thrombolytic therapy as most patients presented early after the onset of chest pain. The earlier the patients received thrombolytic therapy the greater was the ST resolution and further the lesser the complications which would be expected. In view of the low overall mortality statistically significance was not observed in relation to difference between the two groups.In the present study ST resolution occurred in 75% of patients in the first hour and in 82% of patients approximately in the second and third hours. The extent of ST resolution was comparable to the studies done by Ahmad and Ishaq and Lennen.(11) More Indian studies are needed to compare the difference in the extent of ST segment resolution in the Indian population as compared to the Western population. In the study done by Purcell, 1997, it was seen that 50% decrease in maximal lead ST elevation identified patients with a lower prevalence of left ventricular ejection fraction, less than 40% at 36 days and the 60 minute ECG had the highest sensitivity for this clinical outcome.(10) In the same study it was seen that failure of ST resolution was associated with larger left ventricular volumes and lower ejection fractions.In the present study it was seen that at each of the time points, 60 minutes, 120 minutes and 180 minutes patients with failure of ST segment resolution had a higher proportion having LVEF <40% and higher left ventricular dimensions as compared to those who achieved ST resolution. These findings were comparable to the studies done earlier which were quoted above.The relationship between arrhythmias and reperfusion has remained controversial. Some authors have reported a close association between reperfusion and the occurrence of ventricular arrhythmias (Goldberg et al, 1983). (12) In the present study 28% of patients among the group with ST resolution had arrhythmias against 13.4% arrhythmias in patients in group 2 who did not achieve ST resolution. These arrhythmias were probably reperfusion arrhythmias and occurred in a larger percentage of ST resolved patients as compared to those with no ST resolution.Previous studies such as that done by Fibrinolytic Therapy Trialists (FTT) collaboration group, 1994 (9) and (13) showed a proportional reduction in mortality in those who presented soon after MI and it was also seen in other studies such as the GUSTO investigators 1993 (14) and the study by Purcell et al, 1997. (10)So early reperfusion contributed to lesser mortality.In the present study the overall mortality was 4.1% in those who achieved ST resolution against 4% in those who did not achieve ST resolution.The reasons for the low mortality in the present study was effective thrombolytic therapy

and early treatment has markedly decreased the mortality of patients treatment with thrombolytic therapy for acute myocardial infraction.

VII.   CONCLUSIONS

Thus it can be concluded that failure of ST segment resolution is a predictor of poor clinical outcome in patients treated with streptokinase for acute myocardial infarction and those patientswithout ST resolution had lesser left ventricular ejection fractions and higher incidence of complications such as left ventricular failure. Those patients in group 2 with No ST resolution had lesser incidence of reperfusion arrhythmias. A study involving a larger number of patients may have shown effects in better way.

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