RESEARCH ARTICLE

Clinical Markers of Reperfusion in Patients with Acute Myocardial Infarction and Its Prognostic Significance

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ABSTRACT

Introduction: Coronary artery disease (CAD) is a major cause of mortality worldwide. Thrombolysis in the treatment of acute myocardial infarction (AMI) is a landmark event in the management as it has changed the outcomes. Clinical signs after thrombolysis in AMI may have a better correlation with functional reperfusion than the isolated image of angiographic patency.

Aims and objectives: To study successful clinical reperfusion (SCR) noninvasively using clinical markers of reperfusion. To evaluate the prognostic value of clinical markers of reperfusion in predicting early (30 days) prognosis after thrombolysis in AMI. To observe the effect of age, location of MI, presence of previous infarction, Killip's class at admission, and presence of clinical reperfusion assessed noninvasively on early (30 days) prognosis after AMI.

Materials and methods: All the patients were thrombolyzed (using streptokinase). Successful clinical reperfusion was defined by the presence of at least two of the following criteria at 2 hours of starting treatment: (1) Significant relief of pain (50% or more), (2) 50% or more reduction in sum of ST segment elevation, (3) abrupt initial rise of creatine kinase MB (CK-MB) level, more than two-fold over upper normal or baseline values.

Results: Duration of symptoms (min) mean ± SD was nearly the same in two groups (94.80 ± 13.68 *vs* 96.19 ± 17) but early thrombolysis resulted in better outcome (0.01 S, p < 0.05). killips class at admission (KAD) > OR = 2, n (%) led to worsened fate of thrombolysis. Death n (%) occurred in 7 (8.75%) patients with 1 (1.25%) from SCR (+) group and 6 (7.5%) from SCR (–) group (0.01 S, p < 0.05).

Conclusion: It is concluded that Killip's class at admission of more than or equal to two and absence of SCR are the predictors of mortality after thrombolysis. Absence of SCR defines a group of patients with poorer prognosis after thrombolysis and in such patients alternative strategies of reperfusion should be considered.

Keywords: Coronary artery disease, Reperfusion, Streptokinase, Thrombolysis.

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INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality worldwide. It is predicted that CAD resulted in 1.46 million deaths, which is 14% out of a total of 10.3 million deaths in year 2004.[1] Coronary heart disease is forecast to be the most common cause of death globally, including India, by 2020.[2] Introduction of thrombolysis in the treatment of acute myocardial infarction (AMI) was a landmark event in the management of AMI as it has changed the outcomes after AMI.[3,4] It has been convincingly demonstrated that early opening of infarct-related artery is associated with the limitation of the infarct size, preservation of left ventricular function, and better clinical outcome.[5] Reduction in chest pain after thrombolysis has been shown to correlate with angiographically assessed patency and can be used as clinical marker of reperfusion.[6] ST resolution after AMI is influenced by coronary artery status and achievement of early ST resolution is marker of reperfusion.[7,8] Washout of creatine kinase MB (CK-MB), i.e., released from injured myocytes occurs after restoration of coronary artery patency. Hence rapid peaking of CK-MB after thrombolysis can be considered as marker of successful reperfusion.[9] Because angiography is not available in every hospital, there is an increasing interest in simple noninvasive tests of patency assessment.[10] Furthermore, clinical signs after thrombolysis in AMI may have a better correlation with functional reperfusion than the isolated image of angiographic patency.[11]

This opportunity was therefore undertaken to study the success of reperfusion using noninvasive clinical criteria of reperfusion and evaluate prognostic value of clinical markers of reperfusion in predicting short-term (30 days) outcome after AMI in rural setup. Our aim is to study successful reperfusion noninvasively using clinical markers and its prognostic value in predicting early (30 days) outcome after thrombolysis in AMI. We have also observed the effect of age, location of myocardial infarction (MI), presence of previous infarction, Killip's class at admission, and presence of clinical reperfusion assessed noninvasively on early (30 days) prognosis after AMI.

MATERIALS AND METHODS

Study Design

This prospective observational study was carried out in patients of AMI presenting within 6 hours of onset of chest pain, admitted in 20-bed ICU and ICCU of Acharya Vinoba Bhave Rural Hospital of Jawaharlal Nehru Medical College, Wardha in Central India from August 2010 to 2012. All the consecutive patient of AMI admitted in ICU were enrolled in this study, which has been approved by Ethical Committee of the Institute.

Patient Selection

Inclusion Criteria

- Patients with H/O of acute onset of chest pain S/O of AMI (of duration less than 6 hours, lasting more than 20 minutes and not relieved by nitrates irrespective of their Killip's class[12]).
- Twelve lead ECG within 6 hours of onset of chest pain S/O AMI in the form of ST elevation of at least 2 mm in contiguous precordial leads and 1 mm in two adjacent limb leads persisted more than 10 minutes after administration of nitrates.

Exclusion Criteria

- Chest pain for more than 6 hours.
- Left bundle branch block in the electrocardiogram before thrombolysis.
- Those with the contraindication to thrombolysis (as per guidelines given by American College of Cardiology).
- Age of patient more than 75 years.

Methods

All the patients were thrombolysed (using 1.5 million International Units (IU) of streptokinase in 100 mL normal saline over 60 minutes). After thrombolysis patients were divided into two groups based on success of thrombolysis ascertained using noninvasive criteria. Those with successful reperfusion were grouped into SCR (+) group and those without it were grouped into SCR (−) group. Both the groups were then followed for next 30 days and are compared. Successful clinical reperfusion was defined by presence of at least two of the following criteria at 2 hours of starting treatment.

- Significant relief of pain (50% or more)
- A total of 50% or more reduction in sum of ST segment elevation.
- Abrupt initial rise of CK-MB level, more than two-fold over upper normal or baseline values.

Follow-up

Patients from both groups were followed up at 24 hours after thrombolysis and then on 7th day, 30th day, and thereafter if possible.

Statistical Analysis

By univariate analysis (chi-square test), the association of mortality rate with various clinical variable was analyzed. The comparison of baseline variables was made by Student's unpaired t-test, chi-square test for continuous and categorical variables respectively. A "p" value of less than 0.05 was considered statistically significant.

RESULTS

Among 80 cases studied, 60 (75%) were males and 20 (25%) cases were female. The male to female ratio was 3:1. The mean age of patients in the SCR (+) group was 55.7 ± 8.63 years, while mean age of patients from SCR (−) group was 54.71 ± 8.84 years (p = 0.95, NS). Baseline characteristics of our patients are shown in Table 1. There was no correlation between age and success of reperfusion. An analysis of risk factors for the CAD in the present work showed smoking as the commonest risk factor, being present in 56.25% of cases. Hypertension was the next common risk factor seen in 55% cases. Diabetes mellitus type 2 was present in 13.75% cases. Obesity was observed in 34 (42.5%) patients. Majority of patients have duration of chest pain between 61 and 180 minutes, i.e., in 31 (38.75%) patients, out of which 25 (31.25%) patients were in the SCR (+) group and 6 (7.5%) patients in the SCR (−) group. Moreover, 35 (43.75%) patients had chest pain ranging between 241 and 360 minutes in duration, out of which 15 (18.75%) patients were in the SCR (+) and 20 (25%) patients in the SCR (−) group. Mean chest pain duration in both the groups is nearly similar, however,

Table 1: Baseline clinical characteristics and variables

Variable	No. of cases	SCR (+)	SCR (−)	p-value
n	80	48	32	–
Age Mean ± SD	66.54 ±27.76	55.70 ±8.63	54.71 ±8.84	0.62 NS, p>0.05
Sex (% Male)	60 (75%)	38 (47.5%)	22 (27.5%)	0.95 NS, p>0.05
Duration of symptoms (min) Mean ± SD	99.80 ±11.15	94.80 ±13.68	96.19 ±17	0.01 S, p<0.05
Previous infarct n (%)	8 (100%)	4 (50%)	4 (50%)	1.00 NS, p>0.05
Anterior MI n (%)	67 (83.75%)	32 (40%)	25 (31.25%)	0.40 NS, p>0.05
KAD>OR = 2 n (%)	18 (22.5%)	6 (7.5%)	12 (15%)	0.02 S, p<0.05
KAD = 4 n (%)	2 (2.5%)	1 (1.25%)	1 (1.25%)	1.00 NS, p>0.05

NS: Nonsignificant

early treatment resulted in better outcome in the form of reperfusion (t* 14.95, p = 0.01). It was observed that maximum, i.e., 62 (77.5%) patients were in Killip's class I at admission, out of which 42 (52.5%) patients were in the SCR (+) and 20 (25%) patients in the SCR (–) group. Eighteen (24%) patients (among Killip's II, III, and IV) out of 80 were in congestive cardiac failure at the time of admission, out of which 6 (7.5%) patients from SCR (+) and 12 (14%) patients from SCR (–) group. Majority of patients had anterior wall MI, i.e., 57 (71.25%) patients, out of which 32 (40%) patients from SCR (+) group and 25 (31.25%) patients from SCR (–) group. Location of MI did not affect fate of thrombolysis. Chi-square = 1.78, p-value = 0.40, NS, p > 0.05. Mean ejection fraction was 53.33 ± 10.15 in the SCR (+) group, while it was 41.59 ± 13.33 in the SCR (–) group (t = 4.605, p = 0.0001). The ejection fraction in the SCR (–) group was significantly less as compared to SCR (+) group.

Successful clinical reperfusion defined by the presence of two or more of the three clinical criteria was present (SCR+) in 48 (60%) cases, while 32 (40%) cases did not have SCR (–) (Graph 1).

Out of 80 cases studied, 7 (8.75%) patients died within 30 days of thrombolysis. Significantly more deaths occurred in the SCR (–) group as compared to SCR (+) group (7.5 *vs* 1.25%, p < 0.05) (Table 2, Graph 2).

ASSOCIATION OF CLINICAL VARIABLES AND MORTALITY RATE

By univariate analysis, Killip's class II or more at admission and absence of SCR (–) were significantly associated with death. Previous MI, anterior MI, age more than 65, however, were not significantly associated with death (Table 3).

Considering Killip's class at admission, mortality rate was lower in patients with class I than in those with Killip's class II or more at admission (p = 0.002). Absence of SCR was associated with higher mortality rate (odds ratio 10.85, 95% confidence interval 1.23–95.09, p = 0.010) (Table 3).
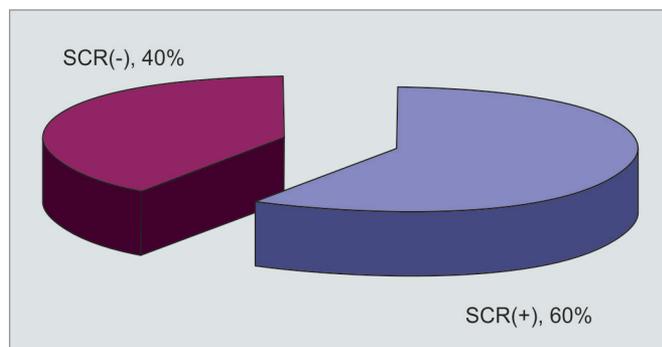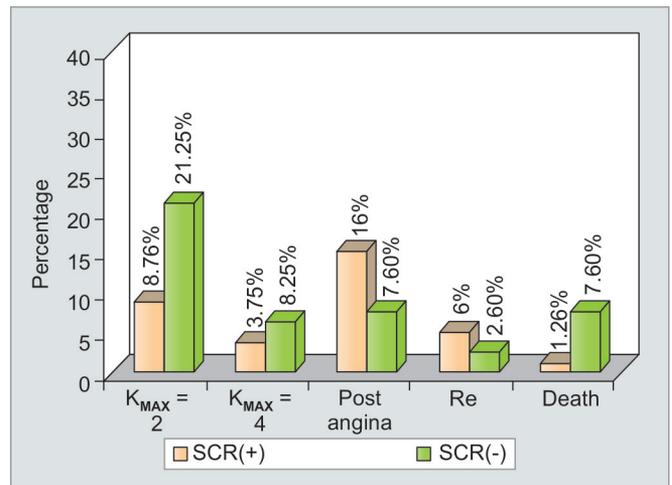

Graph 1: Distribution of Patients in SCR + and SCR –VE Groups

Table 2: Overall and group 30-day events

Event	Overall	SCR (+)	SCR (–)	p-value
Killip's II or more n (%)	24 (30%)	7 (8.75%)	17 (21.25%)	0.01 S, p < 0.05
Killip's MAX = IV n (%)	8 (10%)	3 (3.75%)	5 (6.25%)	0.51 NS, p > 0.05
Post MI Angina n (%)	18 (22.5%)	12 (15%)	6 (7.5%)	0.07 NS, p > 0.05
Re MI n (%)	6 (7.5%)	4 (5%)	2 (2.5%)	0.47 NS, p > 0.05
Death n (%)	7 (8.75%)	1 (1.25%)	6 (7.5%)	0.01 S, p < 0.05

S: Significant; NS: Nonsignificant

Graph 2: Baseline clinical characteristics in two groups

Table 3: Association of clinical variables with 30-day mortality rate

Variables	Chi-square	p-value	OR	95% CI
KAD (≥2 *vs* 1)	14.89	0.002 S, p < 0.05	1.68	0.96–2.95
Absence of SCR	6.68	0.010 S, p < 0.05	10.85	1.23–95.09
Previous MI	0.15	0.69 NS, p > 0.05	1.57	0.16–15.00
Anterior MI	0.92	0.69 NS, p > 0.05	0.37	0.04–3.3
Age > 65	1.09	0.29 NS, p > 0.05	0.40	0.02–7.60

S: Significant; NS: Nonsignificant

Coronary Angiography

Coronary angiography was possible in only 17 cases due to economic constraints. Twelve (70.59%) patients from SCR (+) group underwent coronary angiography, out of which 9 (52.94%) patients had TIMI grade III flow, while 3 (17.65%) patients had TIMI grade II flow in the infarct-related artery.

In the SCR (–) group, 5 (29.41%) patients underwent coronary angiography out of which 2 (11.76%) patients had TIMI grade II flow, 2 (11.76%) had grade I flow, and 1 (5.88%) had grade 0 flow in the infarct-related artery.

There was statistically significant difference in above two groups in terms of presence of TIMI grade II or III flow in relation to success of thrombolysis (chi-square value = 66.52, p-value < 0.0001).

DISCUSSION

Successful clinical reperfusion was observed in 48 (75%) cases and it was absent in 32 (25%) cases. Patients with successful reperfusion were grouped as SCR (+) group and those without it as SCR (–) group. French et al[13] measured ST recovery, and CK-MB before and 60 minutes after commencing streptokinase in 107 patients. At 90 minutes, 56% of patients (95% CI 46–66) had TIMI-3 flow.

Barsottia[14] proved prognostic value of noninvasive markers of coronary reperfusion compared to TIMI 3 flow in patients treated with primary angioplasty. Reperfusion was successful in 87.7% of the patients, and TIMI 3 flow was achieved in 87% patients.

Success of reperfusion reported in the present study using the clinical markers of reperfusion are in accord with those reported by previous studies that range from 50 to 88%.[15]

Our observation in regards to duration of chest pain are similar with findings of Fibrinolytic Therapy Trialist (FTT) Collaborative Group Study.[16] Barsottia[14] reported in their study no significant difference in duration of presentation, i.e., 4.8 ± 2.7 *vs* 4.07 ± 06 hours in the SCR (+) and SCR (–) group respectively.

Mean age of the population in this study was 57.40 ± 8.21 years. Youngest patient was 34 years old, while oldest patient had an age of 70 years. Gupta et al[17] reported 138 patients with the age of patients ranging from 32 to 84 years with mean age of 62.8 years. The mean age of patients in the present study is comparable to that reported in the earlier studies.

In the present study, 60 (75%) males and 20 (25%) females were studied. The male to female ratio was 3:1. Moreover, Johanson et al[18] worked on dynamic model forecasting myocardial infarct size before, during, and after reperfusion therapy by using some of the prognostic criteria's observed to have females is to male ratio 2.9:1. In the present study, the finding regarding male is to female ratio is similar to studies mentioned.

Killip's class II or more were present in 18 (22.5%) patients, out of these, 6 (7.5%) were from SCR (+) group and 12 (15%) patients were from SCR (–) group. There was significant difference in these two groups in terms of occurrence of Killip's class II or more (p = 0.02 S). Ipparaguirre et al[6] reported 90.8% of their patients in Killip's class I at the time of admission. Cardiac failure at admission was present in 9.2% of patients with 5.2% of patients from SCR (+) group and 16.2% patients from SCR (–) group (p < 0.001). Thus cardiac failure at admission was more frequent in the SCR (–) group as compared to SCR (+) group.

Among the patients of anterior wall infarction, 32 (40%) patients were from SCR (+) group and 25 (31.25%) patients were from SCR (–) group (p = 0.99, NS). Thus the two groups did not differ in terms of occurrence of anterior infarction. Barsottia[14] reported that anterior wall infarction was present in 47.2% of patients from SCR (+) group and 83.3% patients from SCR (–) group. Thus the two groups differ in terms of occurrence of anterior infarction (p < 0.05), however, this finding is dissimilar to the finding of present study.

In the present study, the SCR (+) group had mean left ventricular ejection fraction of 53.33 ± 10.15, which was significantly higher as compared to that in the SCR (–) group in which it was 41.59 ± 13.33. (p = 0.0001). The findings in the present study in terms of ejection fraction is similar to the studies reported by Ong et al,[19] Silber et al,[20] and Matetzky et al.[21]

Within 30 days of thrombolysis, 24 (30%) patients had heart failure, out of which 7 (8.75%) patients were in the SCR (+) group and 17 (21.25%) patients in the SCR (–) group. Thus, occurrence of heart failure was significantly more in the SCR (–) group as compared to SCR (+) group (p < 0.05).

Table 4: Comparison of 30 days outcomes in the present study to those with the earlier studies

Event		Barsottia et al[14] (%)	Ipparaguirre et al[6] (%)	Matetzky et al[21] (%)	Present study (%)
$K_{max} >/= 2$	Total	16.6	15	4.32	30
	SCR (+)	NA	10.5	3.7	8.75
	SCR (–)	NA	23.1	5.55	21.25
$K_{max} = 4$	Total	NA	4.9	NA	10
	SCR (+)	NA	0.5	NA	3.75
	SCR (–)	NA	12.8	NA	6.26
Post MI angina	Total	16.02	16.8	NA	22.5
	SCR (+)	NA	20.5	NA	15
	SCR (–)	NA	10.2	NA	7.5
Re MI	Total	11.5	3	12.96	7.5
	SCR (+)	NA	3.3	15.74	5
	SCR (–)	NA	2.5	3.7	2.5
Death	Total	3.65%	8.2	1.85	8.75
	SCR (+)	0.79	3.8	0	1.25
	SCR (–)	22.2	16.2	2.77	7.5

Equal or higher occurrence of postinfarction angina and recurrence of MI in the group with SCR are comparable with the group without it in the present study as well as in the studies by Ipparaguirre et al,[6] Matetzky et al,[21] Simoons et al,[22] The GUSTO investigators,[23] and Barsottia.[14]

In the present study, the overall mortality was 7 (8.75%), out of which 1 (1.25%) patient in the SCR (+) group, while 6 (7.5%) patients in the SCR (–) group. Difference in the mortality in the two groups was statistically significant (p < 0.01). The finding of mortality rate in the present study, moreover, is comparable to that in the studies by Johanson et al,[24] Matetzky et al,[21] Corbalan et al,[25] and Barsottia.[14]

Coronary angiography was possible in only 17 cases due to economic constraints. Twelve patients from SCR (+) group underwent coronary angiography. Out of these, 9 patients had TIMI grade III flow in the infarct-related arteries, while 3 patients had TIMI grade II flow in the infarct-related artery. In the SCR (–) group, 5 patients underwent coronary angiography with 2 patients having TIMI grade II flow, 2 having grade I flow, and 1 having grade 0 flow in the infarct-related artery. There was statistically significant difference in these two groups in terms of presence of TIMI grade II or III flow (p < 0.05).

These observations are similar to French et al[13] and Barsottia[14] suggesting higher TIMI flow in successfully reperfused patients, and thus explaining the importance of clinical markers of reperfusion.

CONCLUSION

The overall occurrence of SCR in the present study was 60%, while 40% patients did not have SCR. It is concluded that Killip's class at admission of more than or equal to two and absence of SCR were the predictors of mortality after thrombolysis. Mortality rate was very high in patients without SCR than in patients with SCR. It is further advocated that all patients of AMI who receive thrombolysis should be assessed at the end of 2 hours for these simple, noninvasive clinical markers of reperfusion. Absence of SCR defines a group of patients with poorer prognosis after thrombolysis and in such patients alternative strategies of reperfusion should be considered.

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