CLINICAL STUDY

Predicting Clinical Outcome in Diabetics versus Nondiabetics with Acute Myocardial Infarction After Thrombolysis

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ABSTRACT

Acute myocardial infarction can be considered as a potential epidemic for mankind (WHO 1982). Diabetes mellitus is one of the 6 primary risk factors identified for myocardial infarction. The aim of our study was to correlate the incidence of complications with diabetes by using ST segment resolution as a tool, thereby re-enforcing the role of incomplete ST resolution as a marker of worse clinical outcome in cases of diabetes with ST-elevated myocardial infarction in our population.

Keywords: Acute myocardial infarction, thrombolysis, ST segment elevation, reperfusion

The acute coronary syndrome includes unstable angina, non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI). Diabetes mellitus is one of the 6 primary factors identified for myocardial infarction (MI), others being dyslipidemia, smoking, male gender, hypertension and family history of atherosclerotic arterial disease. Diabetes mellitus is a metabolic disorder which increases the rate of atherosclerosis progression of vascular occlusion.[1] Even after prompt thrombolysis, the aftermath of diabetic patients is still worse than the nondiabetics, indicating impaired post-thrombolysis left ventricular function and prognosis.

The aim of thrombolysis in acute MI is early and complete myocardial reperfusion.[2] Incomplete or failed reperfusion is associated with increased risk of complications. Analysis of ST segment resolution on electrocardiogram (ECG), after fibrinolytic therapy, in cases of STEMI, offers an attractive and cost-effective solution to assess coronary reperfusion. Whereas coronary angiogram is a marker for epicardial reperfusion, ST segment resolution offers a better reflection of microvascular reperfusion. Although successful thrombolysis of the epicardial vessel is necessary for good prognosis, but the microvascular flow more strongly correlates with the outcome. ST segment is, therefore, a better indicator of prognosis, and provides information, which cannot be assessed on basis of coronary angiogram alone.[3,4] In fact, Schröder et al,[5] reported that absence of ST segment resolution was the most powerful independent predictor of early mortality (p = 0.0001).

ST resolution can also be used as a tool to identify candidates for early invasive procedures such as percutaneous transluminal coronary angioplasty (PTCA), who are at risk of developing complications because of nonresolution of ST segment after initial thrombolytic therapy.[6] Since, ECG is widely available even in developing nations, it is important to establish its effectiveness as a tool for assessing reperfusion as it will offer the cheapest alternative for assessing recovery and myocardial salvage.

MATERIAL AND METHODS

The prospective study was conducted at Sree Balaji Medical College and Hospital, Chennai from June 2015 to October 2015. All cases of acute MI with the diagnosis based on the World Health Organization

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(WHO) criteria i.e., presence of any 2 of the following were included.

- Chest pain consistent with acute MI of less than 24 hours duration.
- Electrocardiography changes i.e., ST segment elevation >0.2 mV in at least 2 contiguous chest leads or >0.1 mV in at least 2 contiguous limb leads.
- New or presumably new left bundle branch block on ECG.
- Raised levels of cardiac enzymes creatine phosphokinase-MB more than double of the reference value or positive troponin I test done with commercially available kits of trop I.

These patients came within 12 hours of chest pain and received streptokinase on presentation. Patients coming after 12 hours of chest pain and patients suffering from type 1 diabetes mellitus were excluded.

The study population was divided into two groups: Group A, nondiabetics (n = 50) and Group B, diabetics (n = 50).

Only those patients who were known cases of diabetes or in whom it was established during hospital stay by repeated blood glucose estimation, were included in Group B.

A detailed history was taken, particularly of age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension and family history of ischemic heart disease. Complete physical examination of patients was done upon presentation in emergency and important parameters such as pulse and blood pressure were noted. Patients were followed up daily. Pulse, ECG changes and complications, if any, were monitored till death or discharge of the patient. The endpoint was a composite of recurrent ischemic chest pain, heart failure, arrhythmia or death.

Time from onset of chest pain to presentation of patient in emergency was noted through the history. ECG recordings of patients were taken upon presentation in emergency. ST elevation was recorded in millimeters from the lead in which maximum elevation was observed. Injection streptokinase was given intravenously to each patient at a dose of 1.5 million units, diluted in 100 mL of normal saline, in 1 hour.

Repeat ECG was performed after 60 minutes of administration of streptokinase (SK). ST resolution was observed in the lead with the maximum ST elevation. ST resolution was defined as a reduction of >50% ST segment elevation after thrombolysis. Informed written consent of the patient/attendant was taken. Follow-up was conducted for each patient throughout his/her hospital stay. Fasting plasma glucose (FPG) was recorded from all patients, in the morning of day following hospital admission for differentiating new cases of diabetes, stress hyperglycemia and nondiabetic. FPG measurements were repeated in stable condition prior to discharge from hospital. The patients were also assessed for the complications during the follow-up. The major complications assessed were: Recurrent ischemic chest pain, heart failure, arrhythmia and death. Recurrent ischemic chest pain was assessed on the basis of history and ECG; heart failure was assessed on the basis of clinical examination, chest X-ray and echocardiography. Arrhythmia was evaluated on the basis of continuous bedside monitoring of ECG. Tachycardia was defined as pulse rate >100 and bradycardia as ≤50/min.

Statistical Analysis

All data was analyzed by SPSS (statistical package for social sciences) version 12.0 for windows, chi-square test was used to compare the demographic characteristics and completion in both groups with 0.05% level of significance.

RESULTS

A total of 100 patients were investigated in this study, of which 70 (70%) were males and 30 (30%) were females. Table 1 shows the demographic characteristics of the study population at presentation. There was no significant difference in the comorbidities of the two groups with hypertension showing the most significant trend.

Table 1. Demographic Data at Time of Presentation

Demographic characteristics	Nondiabetic (Group A) (n = 50)	Diabetic (Group B) (n = 50)
Mean age	55.34 ± 14.38	58.30 ± 12.26
Gender		
Male	38 (76%)	32 (64%)
Female	12 (24%)	18 (36%)
Time of thrombolysis in hours	5.88 ± 1.0	5.07 ± 1.3
Hypertension	15 (30%)	26 (52%)
Hypercholesterolemia	10 (20%)	10 (20.2%)
Family history	9 (18.2%)	7 (14.8%)
Smoking	25 (50%)	24 (48%)

DISCUSSIONS

The time to reperfusion and complete reperfusion remain the key determinants for fibrinolysis. Historically, ST resolution has been one of the markers used to access reperfusion in STEMI. Its importance cannot be denied as a prognostic indicator and the results of our study also reinforce this fact. However, its use as a cost-effective marker has been under utilized. Several studies have reported similar angiographic[7,8] or ECG [9,10] success in both type 2 diabetic and nondiabetic subjects, while others have shown that the diabetics have less complete resolution of ST elevation than the nondiabetics.[11] To evaluate this issue, it has been hypothesized that type 2 diabetes might interfere with intravenous thrombolysis effectiveness, as estimated by angiographic or ECG criteria.

In our study, we observed that in nondiabetic MI 84% patients showed complete resolution and 16% showed failed resolution. But in case of diabetic MI, 13.8% patients showed complete resolution and 86% showed failed resolution. In our study, more complete ST resolution was seen in nondiabetic patient (84% vs. 16%, $p < 0.001$), whereas type 2 diabetic subjects presented with significantly higher incidence of failed ST resolution than nondiabetic subjects (88% vs. 14.8%, $p < 0.001$). This significant change in ST resolution between nondiabetic and diabetic group was similar with the study, which showed significant difference between nondiabetic and diabetic patients in relation to complete (35.1% vs. 69.2%, $p < 0.001$) and incomplete (66.8% vs. 32.6%, $p < 0.001$) resolution.[11] Our results are also consistent with a published meta-analysis in which it was shown that type 2 diabetic subjects had less ST resolution after intravenous thrombolysis administration compared with nondiabetic subjects.[7]

Our results showed the frequency of complications in nondiabetics to be 32.9% compared to 79.8% in diabetics ($p < 0.001$), which was substantially higher in the latter. This finding, therefore establishes a direct correlation between diabetics and the frequency of complications, reflected by less complete ST segment resolution in diabetics in our study (86%).

In our study, we noted that there was a significant interaction between diabetic status and failed ST resolution with respect to the occurrence of in-hospital recurrent ischemia ($p < 0.0001$). Recurrent chest pain is the most common complication observed in the study. A study supporting our results showed that there was a significant interaction between diabetics status and treatment strategy with respect to the occurrence of in-hospital recurrent inchemia.[12] In that study, 32.5% diabetics and 22.1% nondiabetics developed recurrent ischemia after fibrinolysis ($p < 0.001$). As shown by another study, diabetic patients may have a greater residual lesion in the infarct-related artery after treatment with fibrinolytics, resulting in a higher rate of recurrent ischemia.

In our results, we observed that the interaction between diabetics status and failed ST resolution with respect to the development of heart failure was significant ($p = 0.025$). Heart failure is the major determinant for prognosis after MI. Since, some patients never had an echocardiography before this hospital admission to rule out prior heart failure, so any indication of heart failure post-thrombolysis was considered a new development. Our results are supported by the findings of a study, which showed that in-hospital heart failure was more common among diabetics after fibrinolysis.[12] In that study, 10% diabetics and 4.2% nondiabetics developed heart failure ($p = 0.001$).

We observed arrhythmias in 56% of diabetic patients as compared to 10% in nondiabetic patients ($p < 0.0001$). The results clearly shows that arrhythmias are less frequent in nondiabetic patients. Failed ST segment resolution was associated with high frequency of occurrence of arrhythmias compared with complete resolution of both diabetics ($p < 0.0001$) and nondiabetics ($p < 0.0001$). Our results are supported by a study in which incidence of AV block and LBBB, detected in half of the dying patients, was 3 times more common in diabetics than in nondiabetics subjects.

In our study, mortality in diabetic group (only patients with failed ST resolution) was 6.4% compared to 0% in nondiabetic group ($p = 0.014$). A study supporting these findings was carried out by Timmer et al. According to their results, diabetes was associated with increased 30-day mortality. Diabetic mortality was 12.4% and nondiabetic mortality 6.9% after thrombolysis at 30-day endpoint. Small sample size of this study limits our conclusions. There was no post-hospital follow-up, so that is another weak factor of this study. Since, the hospital is equipped to deal with life-threatening emergencies, in-hospital death as a complication was not that high in any group.

The negative influence of diabetes on outcome after STEMI has been described previously. Because mortality remains particularly high in patients with diabetes after STEMI, it is important to define optimal treatment strategies including method of reperfusion therapy, in this population. In our study, it was proved that reperfusion failed in a significant proportion of diabetic patients with STEMI in comparison with nondiabetic persons (86% vs. 16%). Similar results were obtained by Zairis et al.[11] They proved that fibrinolysis may be less effective in diabetic patients. Angeja et al[7] showed that microvascular flow is decreased in diabetic patients after fibrinolysis. Possibly, this is associated with increased platelet aggregation and reduced ability to induce endothelium-mediated vasodilation.

The higher risk of adverse events may be caused by enhanced thrombogenicity and impaired fibrinolysis. Percutaneous coronary intervention (PCI) can be a better alternative in diabetics presenting with acute MI. However, the long-term outcome of these patients depends on the extent of coronary disease and residual left ventricular function, as well as the presence of other risk factors. Hence, aggressive secondary preventive measures such as tight glycemic control and lipid-lowering may be just as important as the mode of reperfusion treatment for these patients.

So, due attention is required for the better management of diabetic MI patients. This should, however, be supplemented with further therapies and strategies directed towards the many abnormalities that are associated with diabetes, such as endothelial dysfunction, dysglycemia and coagulation and fibrinolytic disturbances.

Our study was limited by the fact that the prognosis after STEMI is affected by various factors such as age, gender, number of coronary risk factors presented by the patient, use of aspirin within 7 days and number of angina attacks the patient suffered. We could not assess these factors, which correlate strongly with mortality in our study. A multivariate analysis is required to exclude the importance of these confounding factors.

Stress hyperglycemia has a detrimental effect on thrombolytic outcome after acute MI. Diabetes can be differentiated from stress hyperglycemia with certainty only after the acute phase of the infarction. Thus, any attempt to identify undiagnosed diabetes in our study would have been biased because patients must survive the acute phase to be diagnosed. Another limiting factor was the nonrandomized nature of the research and small size of patients included in the study. In addition to this, it was also limited by the fact that it was a single center study.

CONCLUSION

Frequency of in-hospital complications is more in failed ST resolution compared to complete ST resolution, in both diabetics and nondiabetics, post-thrombolysis. Diabetic population, after thrombolytic therapy, has a higher incidence of adverse clinical outcomes than nondiabetics.

Among diabetic patients with acute MI, fibrinolysis was associated with less complete ST segment resolution, suggesting impaired microvascular flow. Abnormal microvascular flow may contribute at least in part to the poorer outcomes observed in patients with diabetes and acute MI.

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