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Thrombolytic effect of streptokinase infusion assessed by ST-segment resolution between diabetic and non-diabetic myocardial infarction patients

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Abstract

Background: *Recently, it has been hypothesized that type 2 diabetes might interfere with acute intravenous thrombolysis effectiveness as estimated by angiographic or electrocardiographic criteria. In our study, we compared the thrombolytic effect of streptokinase infusion between diabetic and non-diabetic myocardial infarction (MI) patients.*

Methods: *In a prospective interventional study, 240 consecutive patients who were admitted to the emergency ward and diagnosed with ST-elevation MI (STEMI) were enroled and classified into diabetics (n = 85) and non-diabetics (n = 155). Streptokinase was given to each patient at a dose of 1.5 million units in 1 h. Twelve-lead ECG was recorded immediately before the start of thrombolytic therapy and at 180 min afterwards for the patients with STEMI. The ST-segment elevation resolution was calculated and stratified as complete resolution (> 70% ST-resolution), partial resolution (30–70% ST-resolution), or failed resolution (< 30% ST-resolution).*

Results: *Complete ST-resolution occurred in 31.6% of diabetic and 51.0% of non-diabetic patients, respectively (p < 0.001). The incidence of partial ST-resolution in diabetic and non-diabetic patients was 40.5% and 40.0%, whereas 27.8% of patients in the diabetic group and 9.0% of patients in the non-diabetic group showed failed ST resolution. ST-resolution was independent of the location of MI. Multivariate analysis showed that diabetes mellitus, as well as higher Killip class and lower ejection fraction, could effectively predict ST-resolution failure.*

Conclusions: *Failure of ST-segment resolution 180 min after streptokinase infusion is notably higher in diabetic* vs *non-diabetic patients. This failure rate is correlated with higher Killip class and lower ejection fraction.* (Cardiol J 2012; 19, 2: 168–173)

Key words: streptokinase, diabetes, failure, ejection fraction

Introduction

The main purpose of thrombolysis in acute myocardial infarction (MI) is early and complete reperfusion. Therefore, incomplete or delayed reperfusion is associated with an increased risk of death and left ventricular (LV) dysfunction. The time to reperfusion and complete reperfusion remain the key determinants for appropriate outcome of cardiovascular events. Although evidence over recent decades has confirmed the improvement in outcomes of cardiovascular disease in the general population by various therapeutic interventions, these benefits have not been paralleled in diabetic patients [1].

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These patients are considerably at risk of major complications and death after acute ST-segment elevation myocardial infarction (STEMI), independent of other risk factors for coronary artery disease [2].

In fact, although thrombolytic therapy might be accompanied by beneficial effects in diabetic patients, the rates of sustained MI, re-occlusion, and mid-term mortality of treated patients remain worse in diabetic than non-diabetic patients [3–6]. This more adverse outcome can be due to the appearance of impaired post-thrombolysis LV function and prognosis [7].

In this context, some studies have found that thrombolytic agents unquestionably reduce the mortality of patients with a STEMI among patients with diabetes, but others have revealed that diabetic patients were less likely to receive thrombolysis, despite having a greater potential for benefit [8–12]. Thus, it is hypothesized that type 2 diabetes might interfere with the effectiveness of acute intravenous thrombolysis, as estimated by angiographic or electrocardiographic criteria [13]. In the current study, we compared the thrombolytic effect of streptokinase between diabetic and non-diabetic MI patients.

Methods

In a prospective interventional study, 240 consecutive patients who were admitted to the emergency ward of the Shafa hospital in Kerman between April 2006 and October 2007 with typical chest pain or other clinical manifestations of MI within 6 h of the onset of chest pain were included into the study. The final diagnosis of STEMI was confirmed using electrocardiogram (ECG) special changes and elevated cardiac enzymes that were checked at the admission time. Included patients had the following criteria: 1) typical chest pain lasting ≥ 30 min; 2) ST-segment elevation ≥ 0.2 mV in two or more contiguous precordial leads (for the diagnosis of anterior wall MI) or in leads V_1–V_3 (for the diagnosis of anteroseptal wall MI) as well as ≥ 0.1 mV in II, III, and aVF leads (for the diagnosis of inferior wall MI) on the admission ECG; 3) increase in serum creatine kinase (CK) level more than twice the normal value. Exclusion criteria were: late presentation, more than 6 h since the onset of chest pain, history of previous MI, not treated with streptokinase, or left bundle branch block (LBBB) pattern in ECG. All patients signed research study informed consent documents, and the study was approved by the Ethics Committee of the Internal Review Board of Kerman University of Medical Sciences.

Demographic characteristics and clinical criteria of the patients were extracted from previously recorded files, as well as face-to-face interviewing if required, and entered into a computerized database. The patients were given self-administered questionnaires about their medical history including general characteristics, coronary artery disease risk factors: opium addiction (consumption of inhalatory opium more than three times per week and/or oral opium daily) [14], current smoking history (regularly smoking a tobacco product/products one or more times per day or having smoked in the 30 days prior to admission) [15], hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic ≥ 90 mm Hg and//or on antihypertensive treatment) [16], diabetes mellitus (symptoms of diabetes plus at least one of the following: plasma glucose concentration ≥ 11.1 mmol/L, fasting plasma glucose ≥ 7.0 mmol/L, and 2-hpp ≥ 11.1 mmol/L) [17], and Killip class.

Streptokinase was given to each patient at a dose of 1.5 million units, diluted in 100 mL of normal saline, in 1 h. Twelve-lead ECG was recorded immediately before the start of thrombolytic therapy and 180 min afterwards for patients with STEMI. Fasting plasma glucose was recorded from all patients on the morning of the day following hospital admission. Participants were classified into two groups: 1) diabetic patients (n = 85), and 2) non-diabetic patients (n = 155).

ST-segment elevation resolution was calculated as the initial sum of ST-segment elevation (on pre-treatment ECG) minus the sum of ST-segment elevation on the second ECG (180 min after streptokinase infusion) divided by the initial sum of ST-segment elevation and expressed as a percentage. Complete ST-resolution (≥ 70% ST-resolution) in patients with acute MI most likely identifies patients with successful reperfusion following streptokinase therapy, and these patients proved to be a very low-risk group with good prognosis. But failed or no ST-resolution (< 30% ST-resolution) identifies patients with failed myocardial reperfusion, which means that these patients have a higher risk for an adverse outcome [18]. However, partial ST-resolution (< 70% to 30%) is related to impairment of reperfusion at the myocardial level, reflecting the unpredictable effect of streptokinase [19, 20]. Thus, the ST-segment elevation resolution was stratified into three categories: a) complete ST resolution (≥ 70% reduction of ST elevation); b) partial ST resolution (< 70% to 30% reduction of ST elevation); and c) failed ST resolution (< 30% reduction of ST elevation).

Table 1. Baseline characteristics and laboratory data in diabetic and non-diabetic patients.

Characteristics	Diabetics (n = 85)	Non-diabetics (n = 155)	P
Male gender	54 (63.5)	133 (85.8)	< 0.001
Age [years]	59.6 ± 9.4	54.2 ± 12.3	< 0.001
History of hypertension	32 (37.6)	35 (22.6)	0.013
Family history of CAD	16 (20.0)	28 (20.0)	0.999
Current smoking	19 (22.4)	79 (51.0)	< 0.001
Opium use	33 (38.8)	92 (59.4)	0.007
Killip class			
I	50 (61.7)	114 (75.5)	
II	24 (29.6)	26 (17.2)	0.177
III	5 (6.2)	5 (3.3)	
IV	2 (2.5)	6 (4.0)	
Heart rate > 100/min	32 (38.1)	25 (16.1)	< 0.001
Systolic BP > 140 mm Hg	30 (36.1)	42 (27.1)	0.148
Diastolic BP > 100 mm Hg	65 (77.4)	118 (76.1)	0.827
LVEF (%)	42.2 ± 9.0	46.7 ± 9.0	< 0.001
Laboratory parameters:			
Fasting blood sugar	220.5 ± 88.0	102.5 ± 16.3	< 0.001
Total cholesterol	214.0 ± 52.1	201.7 ± 60.3	0.105
Triglyceride	190.6 ± 135.9	149.7 ± 92.4	0.007
Low density lipoprotein	115.9 ± 33.1	118.2 ± 38.7	0.777
High density lipoprotein	51.0 ± 25.6	44.3 ± 10.8	0.102
Serum hemoglobin	14.6 ± 1.9	15.9 ± 3.7	0.001
Serum hematocrit	48.3 ± 33.3	47.0 ± 8.9	0.708
Serum platelet	229.9 ± 97.0	222.6 ± 78.5	0.559

CAD — coronary artery disease; BP — blood pressure; LVEF — left ventricular ejection fraction

Statistical analysis

Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's *t*-test for the continuous variables and the χ^2 test (or Fisher's exact test if required) for the categorical variables. Predictors exhibiting a statistically significant relation with ST resolution status in the two diabetic and non-diabetic groups in univariate analyses were taken for multivariate logistic regression analysis to investigate their independence as predictors. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. A p values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Baseline characteristics and laboratory parameters of the two study subjects are summarized in Table 1. Diabetics were older than the non-diabetic participants, and the history of hypertension was more prevalent in the former group. The overall prevalence of current smoking and regular opium use were higher in the non-diabetics. Diabetic patients suffered more from cardiac tachyarrhythmia, and left ventricular ejection fraction (LVEF) was significantly higher in non-diabetics. The two study groups were matched with respect to family history of coronary disease, Killip class, and current measured blood pressure. Regarding laboratory indices, individuals with diabetes had a lower serum hemoglobin level than the non-diabetics, whereas there were no significant differences in the serum levels of total cholesterol and low density lipoprotein between the two groups. Anterior MI appeared in 41.7% of the diabetics and 30.3% of the non-diabetics, so was slightly more frequent in diabetic patients (p = 0.076). Inferior MI was similarly observed in diabetic and non-diabetic groups (32.1% *vs* 39.4%, p = 0.262) (Fig. 1). Figure 2 shows a comparison of ST-resolution at 180 min after streptokinase between non-diabetic and diabetic MI patients, where complete ST--resolution occurred in 31.6% of diabetic and 51.0% of non-diabetic patients, respectively (p < 0.001).

The incidence of partial ST-resolution in diabetic and non-diabetic patients was 40.5% and 40.0%, where 27.8% of patients in the diabetic group and 9.0% of patients in the non-diabetic group showed failed ST resolution. ST-resolution was independent of the location of MI ($p = 0.276$) (Fig. 3). Multivariate analysis showed that diabetes mellitus, as well as higher Killip class and lower EF, could effectively predict ST resolution failure (Table 2).

Discussion

Some researchers have revealed similar angiographic [21] or electrocardiographic [22] successes in both diabetic and non-diabetic patients, while other studies have shown that diabetics have less complete resolution of ST elevation than non-diabetics [23]. To evaluate this issue, it was hypothesized that diabetes might interfere with the effectiveness of intravenous thrombolysis, as estimated by angiographic or electrocardiographic criteria. The present study addressed the thrombolytic effect of streptokinase in type 2 diabetic STEMI patients and compared it with non-diabetic STEMI patients in the same setting.

In a recent study of ST resolution by thrombolytic versus primary coronary intervention [24], it was shown that ST-segment resolution following thrombolytic therapy was: complete 51.9%, partial 26.6% and failed resolution in 21.5% of acute MI patients 90 min after the initiation of fibrinolytic therapy.

In our trial, we obtained similar results in non-diabetic MI patients, where 51.0% of patients showed complete resolution, 40.0% partial resolution, and 9.0% showed failed resolution. But in cases of diabetic STEMI, 31.6% of patients showed complete resolution, 40.5% partial resolution, and 27.8% failed resolution. In our study, more 'complete ST-resolution' was seen in non-diabetic patients, while type 2 diabetic subjects presented with a significantly higher incidence of failed ST-resolution than non-diabetic subjects.

Overall, ST-segment resolution was significantly more complete in non-diabetic than in diabetic patients. Stress hyperglycemia has a detrimental effect on thrombolytic outcome after acute MI. Mortality may increase, especially in non-diabetic patients. 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. Besides, adjunc-

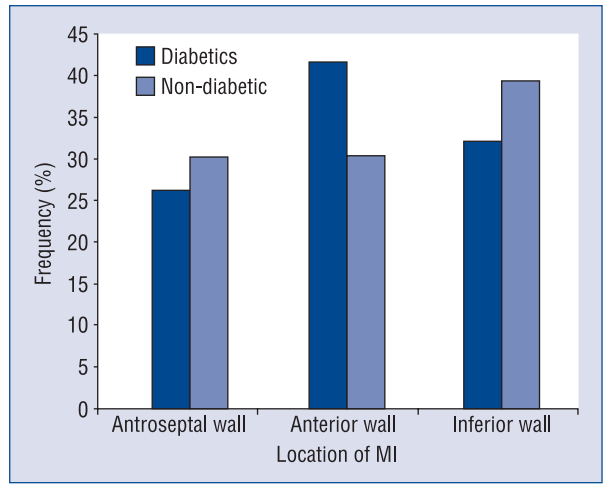

Figure 1. Location of myocardial infarction (MI) in diabetes and non-diabetes.

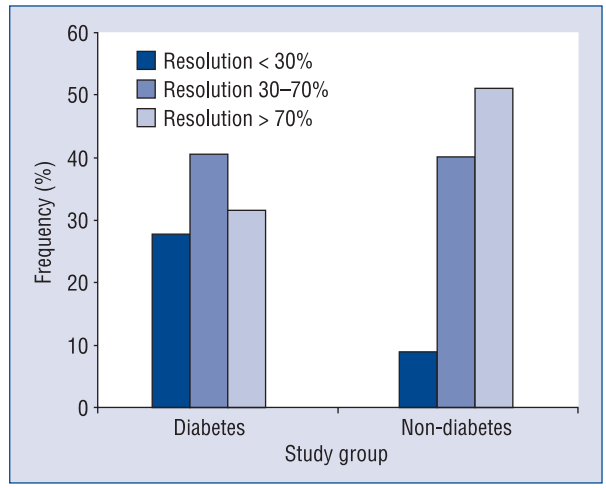

Figure 2. ST-segment resolution in diabetes and non-diabetes.

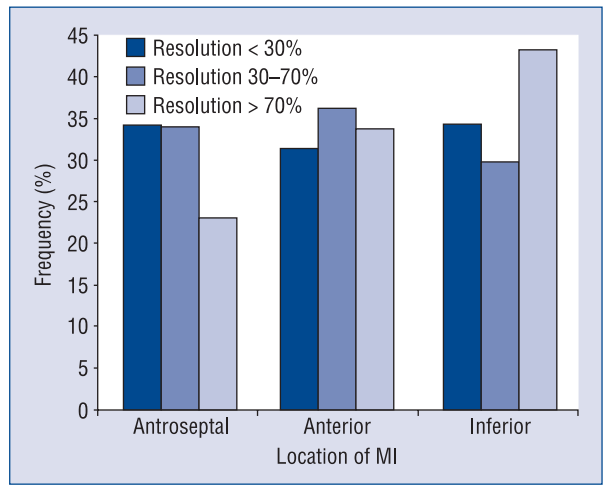

Figure 3. ST-segment resolution in different locations of myocardial infarction (MI).

Table 2. Main determinants of failed ST-segment resolution.

Variable	Univariate p-value	Multivariate p-value	Odds ratio	95% CI
Male gender	0.023	0.590	1.277	0.525–3.111
Diabetes state	< 0.001	0.042	0.477	0.234–0.975
Family history of CAD	0.026	0.102	0.491	0.209–1.151
Heart rate > 100/min	0.001	0.633	0.818	0.360–1.862
Killip class	< 0.001	< 0.001	0.178	0.075–0.422
Opium use	0.048	0.110	1.726	0.833–3.375
Left ventricular ejection fraction	< 0.001	0.038	1.046	1.003–1.091

Hosmer-Lemeshow goodness of fit: $\chi^2 = 6.542$, p = 0.587; CAD — coronary artery disease; CI — confidence interval

tive therapies by aspirin have been suggested as being important for reducing mortality in STEMI. The administration of aspirin just prior to streptokinase infusion might have contributed somewhat to the overall success rate of streptokinase efficacy, but certainly did not influence the relative success/ /failure rates in each time segment.

Other determinants of ST-resolution failure in our study were higher Killip class and lower EF. In some studies, global LV systolic function and survival after thrombolysis have been divergent between diabetic and non-diabetic patients [25, 26]. Impairment of regional LV functions in a non-infarct-related area, which was more common among diabetic patients) [27], and other factors intrinsic to diabetics, such as diastolic dysfunction and myocardial fibrosis, may contribute to the higher observed ST resolution failure rate.

Conclusions

Our study indicates that the failure of ST-segment resolution 180 min after streptokinase infusion is notably higher in diabetic *vs* non-diabetic patients. This failure rate is also correlated with higher Killip class and lower EF.

Conflict of interest: none declared

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