Relationship between admission glucose level and st-segment resolution in stemi patients

Ozgur Kirbas[1], Ozge Kurmus[2], Sina Ali[3], Mehmet Bilge[3]
[1]Department of Cardiology, Yuksek Ihtisas Education and Research Hospital, Ankara,
[2]Department of Cardiology, Tarsus State Hospital, Mersin,
[3]Department of Cardiology, Ataturk Education and Research Hospital, Ankara, Turkey

Abstract

Aim: Admission hyperglycemia is a common clinical condition after acute myocardial infarction (MI). The aim of this study was to study the relationship between admission glucose level and ST-segment resolution in ST-segment elevation MI (STEMI) patients treated with thrombolytics within 12 hours of the onset of chest pain. Material and Method: Data from 232 patients with a diagnosis of first STEMI were analyzed in this prospective study. All of the patients received thrombolytic therapy within 12 hours of the onset of chest pain. The patients were divided into two groups based on the presence of ≥50% ST-segment resolution. Results: Patients with <50% ST-segment resolution had higher admission glucose levels than patients with ≥50% ST-segment resolution (182.57±76.33 mg/dl vs. 150.44±53.95 mg/dl, respectively; p<0.001). Discussion: In the present study, we found that higher admission glucose levels were associated with impaired ST-segment resolution in STEMI patients treated with thrombolytics. Discussion: Our findings suggest that higher glucose values may be related to thrombolytic failure; further studies are needed.

Keywords

Admission Hyperglycemia; Glucose; Acute Myocardial Infarction; ST-Segment Elevation

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Corresponding Author: Ozgur Kirbas, Department of Cardiology, Yuksek Ihtisas Education and Research Hospital, Ankara, Turkey.
GSM: +905336423162 F.: +90 3423352585 E-Mail: omerardakirbas@gmail.com

Introduction

Admission hyperglycemia is a common clinical condition after acute myocardial infarction (MI) [1, 2]. Several studies have demonstrated that admission hyperglycemia is independently associated with increased mortality after acute MI, regardless of treatment modality [3-6]. It has also been reported that non-diabetic patients with acute MI and admission hyperglycemia have higher rates of congestive heart failure, ventricular tachycardia, and atrioventricular block [4-7]. However, the mechanisms of the adverse effects of hyperglycemia are not well known.

Early reperfusion by either thrombolytics or percutaneous coronary intervention (PCI) is the main goal in the treatment of acute MI. However, impaired reperfusion occurs in one-third of ST-segment elevation MI (STEMI) patients treated with fibrinolytic therapy [8-10]. For this reason, predicting patients at risk of failed fibrinolysis is important in determining treatment strategies [8-13].

The aim of this study was to examine the relationship between admission glucose level and ST-segment resolution in STEMI patients treated with thrombolytics within 12 hours of the onset of chest pain.

Material and Method

This prospective case–control study was conducted at Ataturk Education and Research Hospital, Ankara, Turkey, between January and December 2011. The local institutional board of ethics approved the study and signed informed consent was obtained from participants. The universal principles of the Helsinki Declaration were applied.

Data from 232 patients with a diagnosis of first STEMI were analyzed in this prospective study. All of the patients received thrombolytic therapy within 12 hours of the onset of chest pain. STEMI was diagnosed based on a history of a typical chest pain lasting 30 minutes or more and ST-segment elevation of 1 mm or more in at least two contiguous leads or 2 mm or more in leads V1–V3 on electrocardiography (ECG) [7]. All of the patients underwent standard 12-lead ECGs immediately before starting thrombolytic therapy and 90 minutes after the initiation of thrombolytics. Patients with complete left bundle branch block on their admission ECG were excluded. ST-segment measurements were taken 60 ms after the J point in the single lead with maximal ST-segment elevation. At 90 minutes, this lead was examined for the achievement of ≥50% ST-segment resolution. All data were analyzed with an electronic caliper by a single investigator blinded to the study. Traditional variables that have been used to assess response to thrombolytic therapy were relief of chest pain, ST-segment resolution, and reperfusion arrhythmias. Patients with lack of resolution of ST elevation by at least 50% in the worst lead at 90 minutes were considered to proceed with rescue PCI. At the discretion of the treating operator, 118 patients received streptokinase (1.5 million U over 60 min) and 114 patients received t-PA (15mg bolus followed by an infusion of 0.75 mg/kg over 30 min [maximum 50 mg] and an infusion of 0.5 mg/kg over 60 min [maximum 35 mg]). As an adjunctive therapy, 300 mg aspirin was given to all patients on admission and daily thereafter. A loading dose of 300 mg clopidogrel followed by 75 mg once daily was given to patients younger than 75 years of age; the loading dose was not administered to patients older than 75 years [7]. All of the patients received enoxaparin according to body weight, age, and renal function. Patients with a history of significant coronary artery disease, PCI, bypass surgery, oral anticoagulation medicine, bleeding diathesis, malignancy, inflammatory disease, or hepatic or renal insufficiency were excluded from the study.

Statistical Analysis

Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Means and standard deviations for quantitative data and numbers and percentages for qualitative data were computed. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to assess the normal distribution of univariate variables. Non-parametric methods were used to analyze variables that did not have a normal distribution. Chi-square tests were used for categorical variables, where applicable. An independent samples t test was used to compare unadjusted means between groups. Non-parametric variables between groups were compared with a Mann–Whitney U test. Univariate and multivariate logistic regression analyses were used to predict the independent variables of ST-segment resolution. A receiver operating characteristic (ROC) curve was used to determine the sensitivity and specificity of admission glucose level and the optimal cutoff value for predicting ST-segment resolution. The results were considered statistically significant when p values were <0.05.

Results

Baseline clinical, hematological, and biochemical characteristics of the study population are shown in Table 1. The patients were divided into two groups based on the presence of ≥50%

Table 1. The demographics, baseline characteristics, echocardiographic and hematologic parameters of the patients

	ST resolution <0.5 (n=154)	ST resolution ≥0.5 (n=78)	p value
Age, years	58.71 ± 12.33	64.95 ± 11.56	<0.001
Male, n (%)	123 (80.4%)	49 (65.3%)	0.013
Hypertension, n (%)	99 (65.1%)	35 (46.7%)	0.008
Diabetes Mellitus, n (%)	39 (25.3%)	21 (26.9%)	0.398
Smoking, n (%)	52 (34.0%)	38 (50.7%)	0.015
BMI, kg/m^2	24.31 ± 3.06	24.55 ± 3.04	0.588
Systolic BP, mmHg	108.4 ± 17.9	111.8 ± 21.6	0.217
Diastolic BP, mmHg	65.2 ± 10.8	68.9 ± 12.8	0.027
STEMI, anterior localization, n (%)	60 (39.2%)	45 (60.0%)	0.003
Mean LV ejection fraction, %	41.3 ± 10.1	37.7 ± 10.4	0.011
Thrombolytic agent-tPA, n (%)	79 (51.6%)	32 (42.7)	0.203
Hematocrit, %	42.42 ± 4.89	40.63 ± 5.15	0.012
WBC (x10^3/mL)	12.41 ± 11.08	14.63 ± 15.14	0.212
Platelet (x 10^3) - /µL	251.05 ± 71.96	257.57 ± 78.50	0.533
Time to treatment	3.26 ± 2.14	4.35 ± 3.09	0.002
Admission glucose, mg/dL	150.44 ± 53.95	182.57 ± 76.33	<0.001
Peak CK-MB, U/L	117.1 ± 105.4	144.3 ± 97.2	0.078

Data expressed as number (%), mean ± SD. The mean difference is significant at the 0.05 level.
BP: Blood Pressure, BMI: Body Mass Index, CK-MB: creatine kinase-MB, LV: Left ventricular, STEMI: ST elevation myocardial infarction

ST-segment resolution. Of the 232 patients, ≥50% ST-segment resolution was present in 154 patients (66%) and absent in 78 patients (34%). There were statistically significant differences between the two groups in terms of gender, age, hypertension, smoking, localization of MI (anterior vs. non-anterior), ejection fraction, hematocrit, diastolic blood pressure, and time of treatment. There were no statistically significant differences in diabetes mellitus, body mass index, type of thrombolytic agents (e.g., alteplase), and systolic blood pressure, or white blood cell and platelet counts, between the groups. Patients with <50% ST-segment resolution had higher admission glucose levels than patients with ≥50% ST-segment resolution (182.57±76.33 mg/dl vs. 150.44±53.95 mg/dl, respectively; p<0.001) (Table 1). The cutoff value of glucose level on admission for predicting resolution of ST-segment in the entire study population based on ROC analysis was determined to be 148.5 mg/dl, with a sensitivity of 62.7% and a specificity of 60.1% (area under the curve: 0.650; 95% confidence interval (CI): 0.577–0.732; p<0.001) (Figure 1).

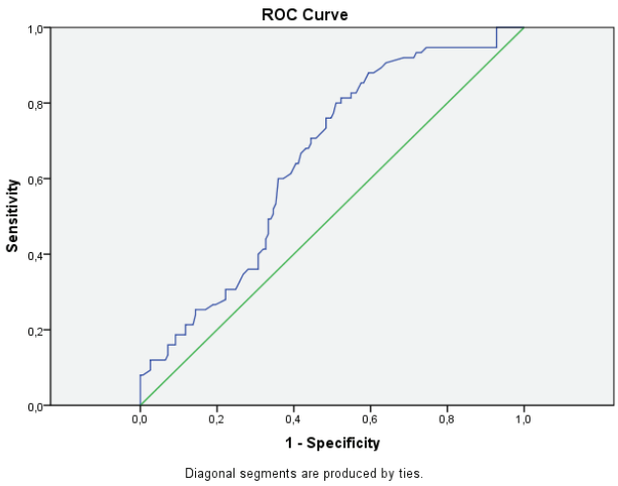

Figure 1. Area under the receiver operating characteristic curve for admission glucose measurements for predicting resolution of ST-segment in the entire study population; optimal cutoff value of admission glucose = 148.5 mg/dl.
AUC=: 0.650; 95% confidence interval: 0.577–0.732; p<0.001).

Table 2. Univariate and multivariate logistic regression analysis of the predictors that can affect on ST segment resolution

	Univariable		Multivariable	
Variables	Odds ratio (95 % CI)	p value	Odds ratio (95 % CI)	p value
Model 1: Admission glucose level as a continuous variable				
Age	0.958 (0.935-0.982	<0.001	0.975 (0.943-1.008)	0.142
Male Gender	2.176 (1.169-4.047)	0.014	1.018 (0.389-2.667)	0.971
Hypertension	2.135 (1.216-3.749)	0.008	1.419 (0.651-3.096)	0.379
Smoking	0.501 (0.286-0.880)	0.016	0.705 (0.289-1.717)	0.441
Anterior MI	0.430 (0.245-0.756)	0.003	0.463 (0.205-1.047)	0.065
LV ejection fraction	1.035 (1.007-1.064)	0.013	1.000 (0.956-1.046)	0.999
Glucose	0.992 (0.988-0.997)	<0.001	0.994 (0.988-0.999)	0.019
Hematocrit	1.074 (1.015-1.136)	0.013	1.064 (0.988-1.146)	0.103
Peak CK-MB	0.998 (0.995-1.000)	0.080	1.000 (0.996-1.004)	0.907
Diastolic BP	0.973 (0.949-0.997)	0.029	0.964 (0.935-0.994	0.019
Time to treatment	0.849 (0.762-0.946)	0.003	0.813 (0.702-0.943)	0.006
Model 2: Admission glucose level as a categorical variable				
Age	0.958 (0.935-0.982	<0.001	0.975 (0.943-1.009)	0.144
Male Gender	2.176 (1.169-4.047)	0.014	0.949 (0.362-2.489)	0.915
Hypertension	2.135 (1.216-3.749)	0.008	1.481 (0.685-3.202)	0.318
Smoking	0.501 (0.286-0.880)	0.016	0.721 (0.298-1.742)	0.467
Anterior MI	0.430 (0.245-0.756)	0.003	0.449 (0.197-1.024)	0.057
LV ejection fraction	1.035 (1.007-1.064)	0.013	1.003 (0.983-1.142)	0.908
Glucose (>148.5)	0.395 (0.224-0.698)	<0.001	0.444 (0.219-0.900)	0.024
Hematocrit	1.074 (1.015-1.136)	0.013	1.59 (0.983-1.142)	0.133
Peak CK-MB	0.998 (0.995-1.000)	0.080	1.000 (0.996-1.004)	0.921
Diastolic BP	0.973 (0.949-0.997)	0.029	0.961 (0.932-0.992)	0.013
Time to treatment	0.849 (0.762-0.946)	0.003	0.811 (0.699-0.941)	0.006

BP: Blood Pressure, CI; confidence interval, MI: myocardial infarction, CK-MB: creatine kinase-MB, LV: Left Ventricular

Univariate and multivariate linear regression analyses were performed to determine the predictors of ST-segment resolution (Table 2). Glucose level >148.5 mg/dl, diastolic blood pressure, and time of administration of thrombolytic agent were shown to be independently associated with ST-segment resolution (odds ratio [OR]: 0.444, 95% CI: 0.219–0.900, p=0.024; OR: 0.961, 95% CI: 0.932–0.992, p=0.013; OR: 0.811, 95% CI: 0.699–0.941, p=0.006, respectively).

Discussion

In the present study, we found that higher admission glucose levels were associated with impaired ST-segment resolution in STEMI patients treated with thrombolytics. Our findings suggest that higher glucose values may be related to thrombolytic failure.

ST-segment resolution, a simple and powerful tool to detect failed thrombolysis, is considered to be a marker of microvascular perfusion [14-19]. Several studies have demonstrated that greater ST-segment resolution was associated with higher rates of infarct-related artery (IRA) patency, less residual stenosis on angiography, smaller infarct size, and better left ventricular systolic function [16, 17, 20]. It has also been shown that ST-segment resolution is associated with lower mortality rate after MI [19, 21]. When complete ST-segment resolution is seen, successful reperfusion appears to have occurred at the tissue level [18, 19]. Patients with persistent ST-segment elevation experience increased morbidity and mortality despite a patent IRA, likely due to microvascular occlusion [19].

Hyperglycemia may be an important contributor to and independent predictor of increased cardiovascular mortality. Stress hyperglycemia in acute MI has been associated with high risk of in-hospital mortality, heart failure, cardiogenic shock, arrhythmias, and no-reflow phenomenon [13]. It has also been shown that long-term prognosis is worse in acute MI patients with admission hyperglycemia [15, 17].

However, the threshold of admission glucose as a predictor of

adverse events in acute MI is unclear, and the exact mechanism of stress hyperglycemia on admission for increased mortality and morbidity in acute MI is not known.

It has been demonstrated that in vitro endothelium-dependent vasodilation and in vivo coronary microvascular responses are impaired by hyperglycemia [15]. It has also been shown that hyperglycemia attenuates nitric oxide-induced effects on collateral blood flow in animals [17]. In another study, it was suggested that elevated plasma glucose might be related to increased production of vasoconstrictor prostanoids by the endothelium [18]. Glucose might play a role in myocardial injury by inducing reactive oxygen species and amplifying inflammatory immune reactions [19, 21]. When catecholamine-induced tissue lipolysis occurs with a release of free fatty acids, the optimum balance of energy of the myocardium deteriorates. Hyperglycemia is associated with increased free fatty acid concentrations, insulin resistance and impaired myocardial glucose use, and worsening ischemia [15]. It has been demonstrated that hyperglycemia is associated with increased platelet aggregation and higher levels of prothrombin fragments and tissue factor [20]. All of these changes occurring in the hyperglycemic milieu can cause a prothrombotic state and altered blood flow, resulting in microvascular dysfunction, myocardial injury, and no-reflow phenomenon, as well as impairment of ST-segment resolution [21].

Conclusion

Admission hyperglycemia in patients who present with STEMI is an independent predictor of impaired ST-segment resolution. Admission blood glucose levels may be used for better risk stratification and prediction of patients at risk of failed fibrinolysis.

Study limitations

Our study has some limitations. First, it is a retrospective study and has a small sample size. Further large-scale studies will be required to validate our results. Because this is a descriptive study, the associations can be interpreted as either cause or consequence; the relationships should be confirmed with longitudinal studies. The unavailability of data regarding glycosylated hemoglobin, insulin levels, and glucose intolerance is another limitation of our study.

Competing interests

The authors declare that they have no competing interests.

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