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Effect of admission glycometabolic state on clinical outcome in non diabetic subjects with acute st segment elevation myocardial infarction

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Abstract *Background and aim:* Glycosylated hemoglobin (HbA1c) is a more stable and accurate parameter of the glycometabolic state than fasting glycemia. However, its role in predicting the prognosis in acute myocardial infarction patients remains unclear with conflicting results from the available data. This study evaluates the effect of admission HbA1c as a parameter of the glycometabolic state on the clinical outcome in non diabetic acute st segment elevation myocardial infarction (STEMI) patients.

Method: Between June 2012 and December 2014, 208 consecutive STEMI non diabetic patients who underwent primary percutaneous coronary intervention (PPCI) were enrolled. Patients were divided according to the HbA1c level into 2 groups 112 patients in group I (HbA1c $\leqslant$ 5.6%) and 96 patients in group II (HbA1c 5.7–6.4%). In hospital and at 6 months major adverse cardiac outcome (MACE) was calculated.

Results: Mean age was 55.9 ± 7.12 years, 149 were men and there was no significant difference regarding baseline characteristics. Post PPCI TIMI III flow was higher in group I ($p = 0.016$), angiographic no reflow was higher in group 2 ($p = 0.003$). No significant difference regarding in hospital MACE ($p = 0.44$). At 6 month follow up MACE was significantly higher in group 2 ($p < 0.001$) and this mainly due to higher incidence of target lesion revascularization (TLR) in group 2 ($p < 0.001$). Multivariate analysis showed that HbA1c is significantly associated with 6 months MACE (hazard ratio 1.9; $p = 0.022$).

Conclusion: Abnormal glycometabolic state assessed by HbA1c at admission in non diabetic STEMI patients was associated with higher MACE incidence at 6 months follow up.

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1. Introduction

Glycosylated hemoglobin (HbA1c) is a stable marker of long term blood glucose control and reflects the average blood glucose concentrations over the previous 8–12 weeks [1]. Elevated

HbA1c is associated with increased cardiovascular risk. It is more closely related to the risk of complications than the other single or episodic measures of glucose levels in diabetic patients [2–5]. In a recent large based population study, it was found that the small elevation in the level of HbA1c in non diabetic patients (i.e. HbA1c < 6.5%), is associated with increased risk of coronary heart disease (CHD) in apparently healthy non diabetic patients irrespective of the fasting blood glucose level [6]. According to the American Diabetes Association (ADA), HbA1c levels between 5.7% and 6.4% indicates prediabetic state [7].

Acute myocardial infarction (AMI) is associated with high risk mortality and morbidity even with the best reperfusion strategy [8]. Stratification of high risk patients is important to improve the prognosis. Previous trials have shown that admission blood glucose had short and long term prognostic value in AMI patients [9,10]. However; the admission blood glucose can't reflect the true glycometablioc state as it is affected by catecholamine release, stress and the patient's last meal. Data on the prognostic role of HbA1c in patients with AMI are derived from studies which differ in patients' selection criteria and therapy (thrombolysis vs. mechanical revascularization). Primary percutaneous coronary intervention (PPCI) has shown significant beneficial protection against death or reinfarction within 6 months AMI [11].

Therefore, we aimed in this study to investigate whether the glycometabolic state measured by the level of HbA1c at time of admission could have a prognostic value for the angiographic and short term clinical outcome in STEMI non diabetic patients undergoing PPCI and whether there is a difference between subgroups of non diabetic patients based on the level of HbA1c.

2. Material and methods

2.1. Patient population

This is a single center observational prospective study. The study included 208 consecutive patients presented by STEMI to the cardiology department of Tanta university hospital during the period from June 2012 to December 2014. All the patients underwent PPCI. The study included males and females aged between 18 and 75 years who have the diagnostic criterion of STEMI i.e. persistent typical chest pain more than 30 min and $\geqslant 2$ mm ST segment elevation in 2 contiguous ECG leads within 12 h of symptom onset. Exclusion criteria included previous use of hypoglycemic drugs or insulin, admission HbA1c $\geqslant 6.5\%$, symptoms more than 12 h, carcinogenic shock and unsuitable coronary anatomy for PCI. The patients were divided into 2 groups based on the level of admission HbA1c according to the ADA guideline, group I (HbA1c $\leqslant 5.6\%$) and group II (HbA1c 5.7–6.4%). A written informed consent was obtained from all participants. The protocol was approved by the local ethics committee.

2.2. Patients' data

Baseline characteristics and demographic data were obtained for all patients. Vital signs, laboratory data and previous disease history were recorded.

2.3. Glycated hemoglobin measurements

Blood samples (5 µL of Capillary blood or anticoagulated venous blood) were obtained at the time of admission and tested with NycoCard Reader II manufactured by Axis-Shield that reports Diabetes Control and Complications Trial (DCCT) aligned values [12] and using National Glycohemoglobin Standardization Program (NGSP)-certified method [13].

2.4. Pharmacotherapy

All the patients received the following regimen before PPCI: (1) clopidogrel loading dose of 600 mg orally, followed by a maintenance dose of 75 mg/day; (2) Aspirin 300 mg followed by 81–325 mg/day; (3) During the procedure, intravenous unfractionated heparin (70 IU/kg), the dose is increased to 100 IU/kg in case glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors are not administrated; and (4) GPIIb/IIIa inhibitor (eptifibatide or tirofiban) unless contraindicated.

2.5. Angiographic procedure

Coronary angiography and PPCI were done through femoral approach. The use of aspiration thrombectomy device was left upon the operator's discretion and only infarct related artery was treated during the index procedure. Pain to balloon time; TIMI flow rate [14] before and after the procedure; and myocardial brush grade (MBG) [15] were assessed.

2.6. In hospital outcome and follow up

MACE was defined as cardiac death, acute myocardial infarction, stent thrombosis or target lesion revascularization (TLR). Academic Research Consortium definition was used to diagnose and grade stent thrombosis [16]. TLR was defined as clinically indicated percutaneous or surgical revascularization of the index lesion during follow-up. Revascularization was considered clinically indicated if there was > 70% diameter stenosis on angiography or > 50% stenosis together with a positive stress test or ischemic symptoms.

Transthoracic echocardiography evaluations were performed after 48–72 h of acute myocardial infarction. Echocardiographic measurements of the left ventricle volumes and ejection fraction (EF%)were performed according to recommendations of the American Society of echocardiography [17]. Upon discharge, all patients were on optimal medical therapy including dual antiplatelet, beta blocker, statin and angiotensin converting enzyme inhibitors (ACEI). Clinical follow up was conducted through office visits and telephone contact during the 6 month follow up period.

2.7. Statistical analysis

The data were analyzed statistically using SPSS version 16. Quantitative variables were presented in the form of mean and standard deviation and description of qualitative variables was presented in their absolute and relative frequencies. Comparison between quantitative variables was carried out by T test of two independent samples and Chi