Influence of admission plasma glucose level on short- and long-term prognosis in patients with ST-segment elevation myocardial infarction

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Abstract

Background/Aim. Hyperglycemia is common in patients with ST-elevation myocardial infarction (STEMI) and is associated with high risk of mortality and morbidity. Relationship between admission plasma glucose (APG) levels and mortality in diabetic and nondiabetic patients with STEMI needs further investigation. The aim of this study was to analyse the short- and long-term prognostic significance of APG levels in patients with STEMI with and without diabetes. Methods. This study included 115 patients with STEMI, 86 (74.8%) nondiabetic and 29 (25.2%) diabetic patients, in which we performed a prospective analysis of the relationship between APG levels and short- and long-term mortality. Results. Comparison of APG levels between nondiabetic (8.32 ± 2.4 mmol/L) and diabetic (10.09 ± 2.5 mmol/L) patients showed statistically significantly higher average APG levels in diabetic patients (p = 0.001). In all patients observed who died either after one month or one year after STEMI, average APG values were significantly higher in comparison with those in survived patients. There was no statistical significance in average APG levels in the diabetic patients with STEMI who died after one month and those who survived (10.09 ± 2.68 vs 10.0 ± 2.51 mmol/L, respectively; p = 0.657), as well as those who died after one year and those who survived (10.1 ± 1.92 vs 10.09 ± 2.8 mmol/L, respectively; p = 0.996). There was, however, statistical significance in average APG levels in the nondiabetic patients with STEMI who died after one month and those who survived (9.97 ± 2.97 vs 7.91 ± 2.08 mmol/L, respectively; p = 0.001), as well as those who died after one year and those who survived (9.17 ± 2.49 vs 7.84 ± 2.24 mmol/L, respectively; p = 0.013). Conclusion. Acute hyperglycemia in the settings of STEMI worsens the prognosis in patients with and without diabetes. Our study showed that nondiabetic patients with high APG levels are at higher risk of mortality than patients with a known history of diabetes.

Key words: blood glucose; myocardial infarction; diabetes mellitus.

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia, with disturbances of carbohydrate, fat and protein metabolism resulting from defects of insulin secretion, insulin action, or combination of both. DM has been rated as an equivalent of coronary heart disease (CHD), and conversely, many patients with established CHD suffer from diabetes or its pre-states. An increased plasma glucose level during stress is a result of sympathetic nervous system activation and a raised production of catecholamines and cortisol that stimulate processes of glycogenolysis, glycolysis and lipolysis. High admission plasma glucose (APG) levels after acute myocardial infarction (AMI) are common and associated with an increased risk of death in subjects with and without known diabetes. Recent data indicate a high prevalence of abnormal glucose metabolism in patients with unknown diabetes at the time of AMI.

Although stress-induced homeostasis disbalance can partly explain the relation between APG levels and outcome, hyperglycemia itself can also be harmful. Thrombotic properties of platelets are increased in a hyperglycemic environment, and this can result in additional cardiovascular complications. Elevated glucose levels may also be associated with increased levels of free fatty acids (FFA). These FFA may increase infarct size, compromise myocardial performance during acute coronary syndrome (ACS), and reduce endothelium-derived vasodilatation in myocardial tissue, limiting myocardial reperfusion. Moreover, recent reports suggest that glucose may be an important mediator in inflammatory responses. One in three patients with suspected ACS had a glucose metabolism disturbance. Hyperglycemia might be associated with an impaired microvascular function after AMI, resulting in a larger infarct size and worse functional recovery. Hyperglycemia is associated with increased risks of heart failure, cardiogenic shock, and death after AMI, but its underlying mechanism remains unknown. APG level in nondiabetic patients with AMI seems to be an independent predictor of a long-term outcome. This indicates that an elevated APG level not only reflects acute stress, but also may be a marker of a disturbed glucose metabolism that worsens the prognosis and requires intervention. Fasting blood glucose (FBG) might be superior to APG in predicting short-term outcomes in patients with AMI. But long-term glycemic control in diabetics may not independently predict mortality suggesting that stress hyperglycemia is of major significance.

During an AMI, plasma FFA levels rapidly increase because of lipolytic effects of catecholamines and/or heparin. Increased FFA levels are toxic to ischemic myocardium and are associated with an increased membrane damage, arrhythmias, metabolic inefficiency, and decreased cardiac function.

The aim of this study was to analyse the short- and long-term prognostic significance of APG level in patients with ST-segment elevation acute myocardial infarction (STEMI) with and without diabetes.

Methods

This study included all patients registered in the Coronary Unit, Department of Cardiology in Internal Clinic, Clinical Center Kragujevac from January, 1 2007 to June 30, 2007. We prospectively studied the relationship between APG level and short- and long-term mortality in patients with STEMI. Serum glucose was determined at admission. A patient survival was measured 28 days and one year after the admission. The patients were defined as having a “previously diagnosed diabetes” (personal history of diabetes defined using ADA 1997 criteria), and as “no diabetes” (those without previously diagnosed diabetes). DM was defined as the use of insulin or glucose-lowering medication on admission, or a diet for diabetes documented in medical history.

The cardiologists used the following criteria for the diagnosis of STEMI: chest pain more than 30 minutes, elevated cardiac enzymes (CPK), and troponin, and development of electrocardiographic (ECG) changes typical for STEMI (persistent ST elevation > 0.1 mV in two or more contiguous leads). A time from the beginning of symptoms to the admission to the Intensive Care Unit had to be less than 48 h. The patients health status was followed-up by phone call interviews with the patients and their families.

Medical data from the patients medical record were collected in a dedicated database. A Statistical Package for Social Sciences Program (SPSS) for Windows XP (version 7.5) was used for all statistical analyses. The data were presented as percentages for discrete variables and as means ± SD for continuous variables. The differences in baseline characteristics were compared using the t-test and χ² test. A p-value < 0.05 was considered statistically significant.

Results

During period observed 393 patients were hospitalized in the Coronary Unit, including 240 patients with ACS. There were 115 patients with STEMI, 29 (25.2%) with diabetes, and 86 (74.8%) without diabetes. The majority of patients in the study were males (69.6%). The mean age of patients with STEMI was 64.25 ± 10.69 years (min 34, max 86 years). The women were older than men (69.2 ± 8.4 vs 62.14 ± 10.91 years, respectively; p = 0.001). Investigation of the patients’ medical history showed that 29 patients (25.2%) had been previously diagnosed with diabetes mellitus, 69 patients (60%) with hypertension, 14 patients (12%) with previous myocardial infarction and 75 patients (65.2%) had a family history of ischemic heart disease. An average APG level of all patients with STEMI in this study was 8.77 ± 2.54 mmol/L. Comparison between APG levels in the nondiabetic (8.32 ± 2.4 mmol/L) and diabetic (10.09 ± 2.5 mmol/L) patients showed a statistically significantly higher average APG level in the diabetic ones (p = 0.001).

An average APG level was statistically significantly higher in the patients who died one month after STEMI than in those who survived (10.1 ± 2.85 vs 8.45 ± 2.37 mmol/L, respectively; p = 0.006). Similarly, an average APG level was statistically significantly higher in patients who died one
year after STEMI than in those who survived (9.4 ± 2.37 vs 8.42 ± 2.57 mmol/L, respectively; \( p = 0.047 \)) (Table 1). A total one-month and one-year mortality of STEMI (one-month and one-year survival) in the patients was 19.1% and 35.6%, respectively.

### Discussion

Recent studies involving non-diabetic patients showed that even mild hyperglycemia in the setting of ACS is also a predictive factor of in-hospital mortality.

<table>
<thead>
<tr>
<th>Time after STEMI</th>
<th>APG level (mmol/L)</th>
<th>Survived patients</th>
<th>Died patients</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-month</td>
<td>8.45 ± 2.37</td>
<td>10.1 ± 2.85</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>One-year</td>
<td>8.42 ± 2.57</td>
<td>9.4 ± 2.37</td>
<td>0.047</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1**: Comparison of average admission plasma glucose (APG) level in all patients depending on one-month and one-year survival after STEMI

There was no statistical significance in average APG level in the diabetic patients with STEMI who died after one month and those who survived (10.09 ± 2.68 vs 10.0 ± 2.51 mmol/L, respectively; \( p = 0.657 \)), as well as those who died after one year and those who survived (10.1 ± 1.92 vs 10.09 ± 2.8 mmol/L, respectively; \( p = 0.996 \)). There was, however, a statistically significant difference in average APG level in the nondiabetic patients with STEMI who died after one month and those who survived (9.97 ± 2.97 vs 7.91 ± 2.08 mmol/L, respectively; \( p = 0.001 \)), as well as those who died after one year and those who survived (9.17 ± 2.49 vs 7.84 ± 2.24 mmol/L, respectively; \( p = 0.013 \)) (Table 2).

Moreover, the new entity called impaired fasting glucose (IFG) (6.1–7 mmol/L) is not only an independent factor of mortality for coronary patients, but has also been associated with doubling of the risk of in-hospital mortality in the setting of ACS. Admission as well as follow-up glycemia are fundamental parameters in ACS for their prognostic value, and as a diagnostic tool in determining the presence of diabetes or IFG. In 2004, the Expert Committee of the American Diabetes Association (ADA) lowered the cutoff point for IFG from 110 to 100 mg/dL on the basis of a new evidence for an increased risk for developing DM and cardiovascular disease. The relevance of this new criterion for IFG to predict

<table>
<thead>
<tr>
<th>APG (mmol/L)</th>
<th>No of patients</th>
<th>Mortality (one-month)</th>
<th>Mortality (one-year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10</td>
<td>16</td>
<td>43.75%</td>
<td>56.25%</td>
</tr>
<tr>
<td>7.8–10.0</td>
<td>21</td>
<td>14.28%</td>
<td>33.33%</td>
</tr>
<tr>
<td>6.1–7.8</td>
<td>34</td>
<td>11.76%</td>
<td>23.53%</td>
</tr>
<tr>
<td>&lt; 6.1</td>
<td>15</td>
<td>13.33%</td>
<td>26.66%</td>
</tr>
</tbody>
</table>

**Table 2**: Comparison of average admission plasma glucose (APG) level in the nondiabetic patients depending on one-month and one-year survival after STEMI

The patients were classified according to the value of APG in four groups: group I with APG >10 mmol/L, group II with APG 7.8–10.0 mmol/L, group III with APG 6.1–7.8 mmol/L, group IV with APG < 6.1 mmol/L. Highest mortality was shown to be in the patient with APG value more than 10 mmol/L.

The patients were also divided into two groups: with and without DM. In the patients with a previous DM, it was shown that the highest one month mortality was in the group I. It was also shown that the highest one-year mortality was in the group II. There was a statistically significant difference in one-month and one-year mortality between these two groups (\( p < 0.01 \)). In the patients without DM (Table 3), highest one-month and one-year mortality was in the group I (> 10 mmol/L).

The most common cause of death in European adults with diabetes is CAD. Their risk is two to three times higher than that among people without diabetes. The combination of DM and previous CAD identifies patients with particularly high risk for coronary death. The relative effect of diabetes is larger in women than men. Many of nondiabetic patients with raised blood glucose have undiagnosed diabetes. Dia-
Nephritic patients may have worse outcomes for many reasons, including more severe CAD, diabetic cardiomyopathy, autonomic dysfunction and decreased endogenous fibrinolytic activity.

APG may be not only the cause of more severe myocardial damage, but also its consequence. Large infarcts are more likely to cause catecholamine release, which affects fatty acid and glucose homeostasis. The catecholamine response is proportional to the severity of infarct, as confirmed by the correlation between APG and heart rate or the Killip class on admission. In a study by Oswald et al., concentrations of cortisol, epinephrine and norepinephrine were the main determinants of APG measured in nondiabetic patients with AMI. In a systematic review and meta-analysis of 15 studies in AMI populations with and without diabetes, Capes et al. showed that in diabetic and nondiabetic patients stress hyperglycemia was associated with an increased risk of inhospital death. Suleiman et al. analysed the additive prognostic value of APG and FBG in a population of 735 nondiabetic patients admitted for AMI. They showed that FBG was a potent indicator of 30-day mortality and appeared more discriminant than admission blood glucose; no long-term data were reported. Foo et al. in a cohort of 2 127 patients presenting with ACS, including STEMI, analysed major complications. APG was an independent and powerful predictor of in-hospital and late mortality in the presence or absence of left ventricular failure and whatever the type of infarction (STEMI or non-STEMI). Recently, Stranders et al. in a retrospective study of 737 nondiabetic patients with AMI found that a 1 mmol/L increase in blood glucose was associated with a 4% increase in long-term mortality. The Multi-national Euro Heart Survey also pointed out that normal glucose regulation is less common than abnormal glucose regulation in patients with unstable CAD. An increased risk of short-term mortality and heart failure has been reported in patients with stress hyperglycemia, as defined by high APG. Suleiman et al. reported that APG between 110 and 121 mg/dL was an independent factor for 30-day mortality.

The results of our study showed that the patients presenting with STEMI who were hyperglycemic on admission represent a high-risk population, even in the absence of an established diagnosis of diabetes. Abnormal glucose metabolism during the acute phase of STEMI is common, and admission hyperglycemia is associated with higher short- and long-term mortality in both diabetic and nondiabetic patients. Moreover, mortality is predicted even more powerfully by admission hyperglycemia in patients without known diabetes. In our study, increased APG was associated with an increase of mortality, in concordance with literature data.

There are several possible causes of hyperglycemia on admission. First, hyperglycemia on admission in nondiabetic patients with STEMI might represent previously undiagnosed DM or pre-existing impaired glucose tolerance, resulting in increased endothelial damage and thus greater risk for micro- and macro-vascular morbidity. Secondly, hyperglycemia on admission might represent a response to acute and severe stress. Our findings suggest that hyperglycemia on admission is a strong risk factor for worse outcome in all patients with STEMI. Measurement of glyceria on hospital admission may be used as an early screening method to detect high-risk patients. According to diabetes guidelines, all patients with CHD and unknown diabetes status should be screened for DM by an oral glucose tolerance test (OGTT). Aggressive monitoring of glucose levels may be beneficial for secondary CAD prevention. Increased APG levels are significantly and independently correlated with poor prognosis after STEMI, especially in nondiabetic patients, that was shown in our study.

In view of all these results, admission hyperglycemia during an acute phase of STEMI and its association with poor outcome represents most likely a combination of previously undiagnosed diabetes, impaired glucose tolerance and a response to acute and severe stress. The data obtained in this study showed that hyperglycemia on admission was associated with a worse outcome for all the patients with STEMI. The impact of a higher APG level on mortality was even more important for nondiabetic than for diabetic patients. Thus, nondiabetic patients with hyperglycemia on admission were at special risk, and may need particular attention. Further investigators should evaluate the effects of acute and intensive glycemic control on reducing mortality.

**Conclusion**

Our study demonstrated that high APG level is common in patients with STEMI and associated with high risk of mortality and morbidity. Nondiabetic patients with high APG have higher risk of mortality than patients with a known history of diabetes. These findings suggest that adequate metabolic control of plasma glucose would be an important treatment target, even in nondiabetic patients.

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