Admission Glucose Level and In-hospital Outcomes in Diabetic and Non-diabetic Patients with ST-elevation Acute Myocardial Infarction

Li Dong-bao, Hua Qi, Guo Jincheng, Li Hong-wei, Chen Hui and Zhao Shu-mei

Abstract

Background  Hyperglycemia on admission is a predictor of an unfavorable prognosis in patients with ST-elevation Acute Myocardial Infarction (AMI). Data concerning associations between an elevated glucose level on admission and other in-hospital complications are still limited.

Methods  A total of 1,137 AMI patients with complete admission blood glucose level (ABGL) analysis were identified and stratified according to ABGL.

Results  A total of 16.1% patients had admission glucose level <5 mmol/L, 36.1% <7 mmol/L, 20.2% <9 mmol/L, 9.9% <11 mmol/L and 17.7% ≥11 mmol/L. Compared with the euglycemia group, both the hypoglycemia and hyperglycemia groups were associated with higher in-hospital mortality. In-hospital mortality of diabetic patients with hypoglycemia (12.2%) was higher than that of diabetic patients with either euglycemia or mild hyperglycemia (11.1%, or 10.7% respectively). The same results were seen in non-diabetic patients. In the logistic regression analysis, admission glucose and cardiac function of Killip grade were the independent predictors of in-hospital death for patients with AMI.

Conclusion  Elevated admission glucose levels are associated with an increased risk of life-threatening complications in diabetic and non-diabetic AMI patients. Compared with the euglycemia group, hypoglycemia was associated with a higher trend of in-hospital mortality.

Key words: acute myocardial infarction, admission glucose, diabetes, mortality

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Introduction

Hyperglycemia on admission has been shown to be a strong predictor of unfavorable prognosis in both diabetic and non-diabetic patients presenting with acute coronary syndromes (1, 2). On the other hand, data concerning the associations between elevated glucose level on admission and in-hospital complications are still limited (2, 3). However, it has also been suggested that a lower glucose level on admission or during hospitalization for AMI may be associated with a worse outcome (1, 4). The purpose of the present study was to assess the impact of admission glucose level on mortality and other in-hospital complications in ST-elevation acute myocardial infarction (AMI) patients in hospital.

Materials and Methods

Study Population

Between April 1995 and May 2005, 1,137 consecutive AMI patients, who were admitted within 12-24 hours after the onset of symptoms, underwent an emergency Percutaneous Coronary Intervention (PCI) or drug therapy or thrombolysis at the Department of Cardiology, Xuanwu Hospital, Capital Medical University, Beijing China. Acute myocardial infarctions were defined by the following char-
acteristics: chest pain consistent with any ongoing myocardial ischemia persisting longer than 30 minutes, ischemic electrocardiographic changes, and a greater than 3-fold increase in serum creatine kinase levels. This study excluded patients with a history of recent surgery or trauma within the preceding 2 months, renal insufficiency (creatinine>106 mmol/L), malignancy or liver cirrhosis, febrile disorders, acute or chronic inflammatory disease on study entry or history of recent infection, previous myocardial infarction (5).

**Study protocol**

We performed coronary angiography using the right brachial or femoral approach to determine the culprit lesion. Primary PCI or fibrinolytic therapy or drug therapy only was performed as a therapy in all AMI patients. Reperfusion was considered successful if balloon angioplasty and/or stent deployment was carried out at the desired site yielding residual stenosis of <50% diameter and Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow. Patients were divided into five prespecified groups based on non-fasting glucose level on admission: Hypoglycemia (<5 mmol/L), Euglycemia(5-7 mmol/L), Mild hyperglycemia (7-9 mmol/L), Moderate hyperglycemia (9-11 mmol/L), Severe hyperglycemia (>11 mmol/L).

Blood samples for measuring white blood cell count, admission glucose (non-fasting), peak of creatine phosphokinase (CPK) and CK-mb, creatine, low-density lipoprotein cholesterol (LDL-C), were taken from a peripheral vessel in the cardiac intensive care unit before the administration of any medication. Left ventricular ejection fraction was measured with Doppler echocardiography during the 3 days after acute myocardial infarction. Patients were considered to have diabetes if they had a previous or current diagnosis of diabetes, regardless of glucose status at admission.

Patients in this study were followed up in-hospital intervals after the AMI event. Rate of death and VT/VF, atrial fibrillation and 2nd to 3rd AV block are included in the clinical information.

**Statistical analysis**

Data are expressed as mean ± SD or frequency. Baseline clinical characteristics were compared by the chi-square test for categorical variables and the analysis of variance test for continuous variables. The unadjusted association between groups of admission plasma glucose and in-hospital mortality was tested with the chi-square test. Logistic regression analyses were used to determine the predictors of mortality in-hospital complications. All p<0.05 were considered statistically significant. Analyses were done using the statistical software SPSS 11.5.

**Results**

**Baseline clinical characteristics**

The mean of admission glucose level of 1,137 patients was 8.67±4.83 mmol/L and 183 (16.1%) patients had admission glucose level ≤5 mmol/L, 410 (36.1%) ≤7 mmol/L, 230 (20.2%) ≤9 mmol/L, 113(9.9%) ≤11 mmol/L and 201 (17.7%) ≥11 mmol/L. A total of 246 (21.6%) patients were classified as diabetic. Patients with higher admission glucose levels were more likely to be male, with more advanced age, and a history of smoking. There were 246 (21.6%) patients with and 891 (78.4%) patients without a history of diabetes. Mean admission glucose was significantly higher in diabetic patients vs. non-diabetic, 12.97±6.05 vs. 7.71±3.89 mmol/L, p<0.0001, and in death patients vs. non-death patients, 11.86±6.25 vs. 8.27±4.45 mmol/L, p<0.0001. There was no difference in the frequency of invasive treatment or fibrinolytic therapy or conservative treatment among study groups (Table 1).

**Association between admission glucose and mortality**

There was a U-shaped relationship between admission glucose levels and in-hospital all-cause mortality in all patients with AMI. Compared with the euglycemia group, both the hypo and hyperglycaemia groups were associated with higher in-hospital mortality. In-hospital mortality of diabetic patients with hypoglycemia (12.2%) was higher than that of diabetic patients with either euglycemia or mild hyperglycemia (11.1% or 10.7% relative increase). The same results were seen in non-diabetic patients (Table 2).

Total in-hospital mortality of patients was 12.3%, and observed mortality was significantly higher in diabetic than in non-diabetic patients (19.1 vs. 10.4%, p<0.001). In-hospital mortality was higher in patients with higher admission glucose levels. Significant mortality difference was observed in diabetic and non-diabetic patients (Table 2).

In logistic regression analyses, independent predictors of in-hospital death for patients with AMI were: age, admission glucose, cardiac function of Killip grade and heart rate and arrhythmia (Table 3).

**Discussion**

The present study has confirmed findings from previous reports that admission hyperglycemia is independently associated with excess mortality in both diabetic and non-diabetic patients presenting with acute coronary syndromes (6).

Capes et al (7) demonstrated that the relative risk of in-hospital death in non-diabetic patients with AMI with admission glucose ≥6.1 mmol/L was 3.9 compared with non-diabetic patients with AMI who were normoglycemic. Among patients with AMI with diabetes, those with admission glucose ≥10 mmol/L had a 70% relative increase in the risk of in-hospital death compared with diabetic patients with normal admission glucose values. Similarly, Foo et al (8) demonstrated a near-linear relationship between higher admission glucose levels and higher rates of cardiac death among 2,127 patients with acute coronary syndromes.
Table 1. Baseline Clinical Characteristics for Whole Patients Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypoglycaemia</th>
<th>Euglycemia</th>
<th>Glucose level on admission (mg/dL)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=183)</td>
<td>(n=410)</td>
<td>Mild HG</td>
<td>Moderate HG</td>
</tr>
<tr>
<td>Age (ys)</td>
<td>62±13</td>
<td>61±12</td>
<td>63±11</td>
<td>64±11</td>
</tr>
<tr>
<td>Male</td>
<td>140(76.5%)</td>
<td>330(80.5%)</td>
<td>155(67.4%)</td>
<td>81(71.7%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>49(26.8%)</td>
<td>27(6.6%)</td>
<td>28(12.2%)</td>
<td>31(27.4%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62(33.9%)</td>
<td>176(42.9%)</td>
<td>118(51.3%)</td>
<td>60(53.1%)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>101(55.2%)</td>
<td>265(64.6%)</td>
<td>134(58.3%)</td>
<td>58(51.3%)</td>
</tr>
<tr>
<td>Time from onset to admission (h)</td>
<td>6.85±6.05</td>
<td>7.51±7.51</td>
<td>6.64±7.15</td>
<td>6.37±5.22</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>78.97±18.56</td>
<td>76.95±16.65</td>
<td>77.82±17.16</td>
<td>77.93±18.03</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>130.67±26.97</td>
<td>134.17±26.97</td>
<td>133.06±29.50</td>
<td>135.43±30.86</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80.78±15.61</td>
<td>81.29±17.20</td>
<td>79.99±15.38</td>
<td>81.91±15.92</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>55.32±9.94</td>
<td>56.43±10.35</td>
<td>54.96±10.99</td>
<td>56.07±11.81</td>
</tr>
<tr>
<td>White blood cell (×10 9)</td>
<td>10.70±4.57</td>
<td>10.51±3.37</td>
<td>11.26±5.06</td>
<td>11.56±3.50</td>
</tr>
<tr>
<td>Peak of CPK (U/L)</td>
<td>1732.29±1444.00</td>
<td>1697.46±1308.13</td>
<td>1718.01±1337.43</td>
<td>1945.25±1429.80</td>
</tr>
<tr>
<td>Killp</td>
<td>122 (66.7%)</td>
<td>282 (68.8%)</td>
<td>138 (60.0%)</td>
<td>61 (54.0%)</td>
</tr>
<tr>
<td>Arhythmic</td>
<td>13 (7.1%)</td>
<td>23 (5.6%)</td>
<td>17 (7.4%)</td>
<td>12 (10.6%)</td>
</tr>
<tr>
<td>All patients</td>
<td>19(10.4)</td>
<td>29(7.1%)</td>
<td>18(7.8%)</td>
<td>21(18.6%)</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>6(12.2%)</td>
<td>3(11.1%)</td>
<td>3(10.7%)</td>
<td>4(12.9%)</td>
</tr>
<tr>
<td>Non-diabetic patients</td>
<td>13(9.7%)</td>
<td>26(6.8%)</td>
<td>15(7.4%)</td>
<td>17(20.7%)</td>
</tr>
</tbody>
</table>

Notes: CPK: Creatine phosphokinase; PCI :percutaneous coronary intervention; VT: Ventricular tachycardia ;VF:ventricular fibrillation; AV: auriculoventricular; HG:high glucose

Table 2. Association between Admission Glucose and Mortality

<table>
<thead>
<tr>
<th>Glucose level on admission</th>
<th>Hypoglycaemia</th>
<th>Euglycemia</th>
<th>Mild HG</th>
<th>Moderate HG</th>
<th>Severe HG</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=183)</td>
<td>(n=410)</td>
<td>(n=230)</td>
<td>(n=113)</td>
<td>(n=201)</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>19(10.4)</td>
<td>29(7.1%)</td>
<td>18(7.8%)</td>
<td>21(18.6%)</td>
<td>53(26.4%)</td>
<td>0.00</td>
</tr>
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<td>6(12.2%)</td>
<td>3(11.1%)</td>
<td>3(10.7%)</td>
<td>4(12.9%)</td>
<td>3(17.9%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Non-diabetic patients</td>
<td>13(9.7%)</td>
<td>26(6.8%)</td>
<td>15(7.4%)</td>
<td>17(20.7%)</td>
<td>22(24.4%)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Notes: HG:high glucose

Cooperative Cardiovascular Project (9), the largest retrospective study of this subject to date, which examined the outcomes of 141,680 elderly patients with AMI, demonstrated a significant 13-77% relative increase in 30-day mortality and a 7-46% relative increase in 1-year mortality depending on the degree of hyperglycemia.

Mechanisms responsible for excessive mortality in patients presenting with AMI and hyperglycemia, especially among patients without previously diagnosed diabetes are still a matter of debate. As admission hyperglycemia is frequently observed in higher risk individuals, including older patients, or diabetic patients, there is the suggestion that elevated glucose levels are only a marker of disease severity (6). On the other hand, there are many observations suggesting a possible direct impact of hyperglycemia on adverse outcomes by various pathophysiological mechanisms.

Previous studies have reported associations between elevated admission glucose levels and lower rates of spontaneous reperfusion and bigger infarct size in AMI (10), and inflammation (11) in acute coronary syndrome patients.
studies have suggested that hyperglycemia has a direct detrimental effect on ischemic myocardium. It has been reported that acute hyperglycemia abolishes ischemic preconditioning and promotes apoptosis. (12, 13) Acute hyperglycemia also decreases nitric oxide bioavailability, impairs endothelial function, increases platelet aggregability, and stimulates coagulation (14). These changes may cause microvascular dysfunction during reperfusion and impaired left ventricular function after AMI (15). Another possible explanation is a paradoxical resistance of diabetic hearts to ischemic challenge. Although controversy exists as to whether diabetic hearts are more or less sensitive to ischemic injury, in vitro studies are more consistent in demonstrating that diabetic hearts are less susceptible to injury after a severe episode of ischemia (16). The high rates of glycolysis during ischemia result in an accumulation of proton, which is exchanged for sodium by the sodium proton exchanger, especially at the onset of reperfusion.

In the present study, we observed that mild to moderate decreasing admission glucose levels were associated with a relative increase in risk of mortality. There was a U-shaped relationship between admission glucose levels and in-hospital mortality. This U-shaped relationship was not restricted to patients with pre-existing diabetes. The prognostic significance of hypoglycemia after AMI is controversial. Svensson et al (17) conducted a study in 713 diabetic patients with unstable angina or non-Q-wave myocardial infarction and found a significantly higher mortality at 2 years in subjects with hypoglycemia (admission glucose <3.0 mmol/L) than in those with euglycemia; however, a causal link between in-hospital hypoglycemia and clinical outcomes ascertained 2 years later is difficult to establish. Kosiborod et al (18) showed that hypoglycemia (admission glucose <3.3 mmol/L) was associated with increased mortality in patients with AMI, but this risk was confined to patients who had spontaneous hypoglycemia (and did not include iatrogenic hypoglycemia). A more recent analysis by Goyal et al (19) showed that both admission and post-admission hypoglycemia (admission glucose ≤3.8 mmol/L) could predict 30-day death in patients with AMI. However, only hypoglycemia on admission predicted death, and this relationship dissipated after admission. Another report from the DIGAMI 2 (Diabetes mellitus, Insulin Glucose infusion in Acute Myocardial Infarction 2) trial (20) showed that hypoglycemia (admission glucose <3.0 mmol/L) during the initial hospitalization was not an independent risk factor for future morbidity or mortality in patients with type 2 diabetes and myocardial infarction. Hypoglycemic episodes were, however, more prevalent in patients at high risk for other reasons.

**Limitations**

Several important limitations of the present study should be acknowledged. First, this was a single-center, non-randomized, and retrospective study with a relatively small number of patients. Second, the admission glucose levels were potentially assessed by different methods, and standardized central laboratory measurements were not available. Third, the time relationship between elevated admission glucose level, in-hospital complications occurrence and mortality was not assessed.

**Conclusions**

Elevated admission glucose levels are associated with an increased risk of life-threatening complications in diabetic and non-diabetic AMI patients. Compared with the euglycemia group, hypoglycemia was associated with a higher trend of in-hospital mortality.

**The authors state that they have no Conflict of Interest (COI).**

**References**

10. Timmer JR, Ottewanger JP, de Boer MJ, et al. Hyperglycemia is an important predictor of impaired coronary flow before reperfu-


