

Relationship between blood glucose on admission and prognosis in patients with acute myocardial infarction treated with percutaneous coronary intervention

Mariusz Gąsior¹, Gabriela Stasik-Pres¹, Damian Pres¹, Piotr Lech¹, Marek Gierlotka¹, Andrzej Lekston¹, Michał Hawranek¹, Mateusz Tajstra¹, Zbigniew Kalarus², Lech Poloński¹

¹ 3rd Chair and Department of Cardiology, Silesian Medical University, Silesian Centre for Heart Diseases, Zabrze, Poland

² 1st Chair and Department of Cardiology, Silesian Medical University, Silesian Centre for Heart Diseases, Zabrze, Poland

Abstract

Background: Diabetes mellitus in patients with myocardial infarction affects in-hospital and late mortality. It has been shown that the glucose level on admission can also affect prognosis. This conclusion was based on an analysis performed on a heterogeneous group of patients, treated not only with percutaneous coronary intervention (PCI) but also with fibrinolysis. Moreover, the threshold values hyperglycaemia for the diagnosis of were also variable.

Aim: To assess whether glucose level on admission affects in-hospital and one-year prognosis in patients with ST-segment elevation myocardial infarction (STEMI) treated with PCI.

Methods: Consecutive patients with STEMI treated with PCI were included in the analysis. Patients with STEMI complicated by cardiogenic shock were also included. Three groups according to the glucose level on admission were analysed: group I – <7.8 mmol/l (140 mg/dl), group II – 7.8-11.1 mmol/l (140-200 mg/dl), and group III – ≥11.1 mmol/l (200 mg/dl).

Results: The incidence of diabetes mellitus in the total group (1027 patients) was 26.1%, and of cardiogenic shock – 9.2%. Group I consisted of 472 patients, group II – 307 patients, and group III – 248 patients. Compared with normoglycaemic patients, those with elevated glucose level were older, more often female, had more often hypertension, diabetes mellitus, cardiogenic shock, were more often treated with fibrinolysis before PCI but were less often smokers. Multivessel disease and initial patency of the infarct-related artery (TIMI 0-1) were more often observed in patients with higher glucose level. A trend towards a higher incidence of reocclusion was also more often present in patients with increased glucose level. Moreover, mean creatine kinase concentration was the highest and the left ventricular ejection fraction was the lowest in group III. During the in-hospital stay, the complication rate was as follows: stroke (1.1% vs. 1.3% vs. 4.4%), and mortality (2.8 vs. 4.9 vs. 13.3%) in groups I, II, and III, respectively. The same tendency was observed during the one-year follow-up period: stroke (1.3 vs. 2.9 vs. 6.9%), mortality (6.4 vs. 9.1 vs. 22.6%). The 1 mmol/l (18 mg/dl) increase of the baseline glucose level among various risk factors was an independent prognostic factor of higher -year mortality (HR=1.06; 95% CI 1.02-1.09). Diabetes mellitus did not affect prognosis among patients included in the analysis.

Conclusion: Elevated glucose level on admission is associated with adverse prognosis in patients with STEMI treated with PCI.

Key words: myocardial infarction, diabetes mellitus, glucose level on admission

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Address for correspondence:

Mariusz Gąsior MD, III Katedra i Oddział Kliniczny Kardiologii, ŚUM, Śląskie Centrum Chorób Serca, ul. Szpitalna 2, 41-800 Zabrze, tel.: +48 32 273 23 16, e-mail: mariuszgasiors@poczta.onet.pl

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Introduction

Introduction of percutaneous coronary intervention (PCI) significantly improved prognosis after myocardial infarction (MI) [1]. This results from a higher rate of TIMI (*Thrombolysis in Myocardial Infarction*) grade 3 flow after PCI compared to fibrinolysis [2]. The presence of diabetes mellitus in patients with MI increases in-hospital and long-term mortality regardless of therapy used [3, 4]. There are reports available suggesting that blood glucose (BG) in the acute stage of MI may determine prognosis. This conclusion is based on reports analysing various groups of patients. Reported in literature studies included both patients with ST-segment elevation MI (STEMI) and other types of acute coronary syndromes, however, these data were obtained for patients treated with fibrinolysis and PCI. Additionally, BG levels on admission indicating hyperglycaemia were variable. These differences may lead to conflicting outcomes [5-12]. Only a few available reports have investigated the relationship between BG on admission and prognosis in patients with MI regardless of the diagnosis of diabetes mellitus [13-16]. The aim of this study was to determine the prognostic value of BG level checked on admission on the in-hospital and 12-month outcome in patients with acute MI treated with PCI.

Methods

Study group

The analysis involved consecutive patients with STEMI treated with PCI in 1998-2003 at our department, in whom BG level was measured on admission. Patients with MI complicated with cardiogenic shock were also enrolled. Cardiogenic shock was diagnosed based on clinical and haemodynamic criteria. Haemodynamic criteria included: systemic systolic blood pressure <90 mmHg or drop of 30 mmHg from the baseline for at least 30 minutes without administration of inotropic agents or intraaortic balloon pumping (IABP) or systolic blood pressure >90 and <110 mmHg on inotropic agents or IABP.

PCI procedure

Urgent coronary angiography followed by PCI was performed in the following patients: with persistent angina ≥ 30 minutes, with electrocardiographic signs of MI, i.e. ST elevation of ≥ 0.1 mV in at least two limb leads or ST ≥ 0.2 mV in at least two precordial leads or new left bundle branch block, with pain to intervention time up to 12 hours (or 18 hours in patients with cardiogenic shock). Prior to coronary angiography, patients received oral 300 mg of acetylsalicylic acid (ASA), intravenous 5000-10000 units of heparin and 2.5-5.0 mg morphine

(if not given earlier). Epicardial blood flow was evaluated using TIMI scale [17]. After coronary angiography and qualification for stent implantation the patients were given 300 mg of clopidogrel. The IABP was used depending on patients' clinical condition. Effective PCI was defined as TIMI grade 3 flow and presence of residual stenosis of $\leq 30\%$ without evidence of blood flow limiting dissection.

In-hospital treatment

In-hospital therapy included oral ASA 150 mg daily, beta-blockers, angiotensin-converting enzyme inhibitors and statins, if not contraindicated. Patients undergoing stenting were given oral 250 mg ticlopidine b.i.d. with up to 8-week continuation. Urgent coronary angiography was performed in each patient with recurrent angina and concomitant ST elevation. If reocclusion or significant stenosis of the culprit artery was confirmed, re-PCI was performed.

Patient groups according to blood glucose levels

Patients were divided into three groups according to the BG level on admission and regardless of previous diagnosis of diabetes mellitus. The first group (group I) comprised patients with BG on admission <7.8 mmol/l (140 mg/dl); the second group (group II) comprised patients with BG 7.8-11.1 mmol/l (140-200 mg/dl); and the third one (group III) comprised patients with BG ≥ 11.1 mmol/l (200 mg/dl). These groups were compared with respect to the selected parameters of in-hospital and 12-month follow-up.

Diabetic patients were selected using the following criteria: medical history (documented diabetes treated with insulin or oral hypoglycaemic drugs or diet) and elevated BG during hospitalisation (at least two fasting BG measurements of ≥ 7 mmol/l (126 mg/dl) or ≥ 11.1 mmol/l (200 mg/dl) during oral glucose tolerance test (OGTT)). These criteria are consistent with the guidelines on diagnosis of diabetes mellitus [18].

Statistical analyses

Continuous data are shown as a mean \pm standard deviation. Statistical significance of differences between the means was assessed using ANOVA. Qualitative parameters were compared using χ^2 test (if expected frequency was below 5, the Yates' correction applied). The effects of individual parameters on mortality were analysed with the Kaplan-Meier method, log-rank test and Cox proportional hazard model; the results are shown as the hazard ratio (HR) and 95% confidence interval (CI). Results were found statistically significant if

Table I. Clinical characteristics of the studied patients

Parameters	Group I blood glucose <7.8 mmol/l (140 mg/dl)	Group II blood glucose 7.8-11.1 mmol/l (140-200 mg/dl)	Group III blood glucose ≥11.1 mmol/l (200 mg/dl)	p
Number of patients [n]	472	307	248	
Age [years]	55.7±10.7	59.5±10.7	62.0±9.85	0.00001 # &
Females [%]	20.3	29.6	42.3	0.00001 * &
Arterial hypertension [%]	47.0	56.0	66.3	0.00001 # &
Hypercholesterolaemia [%]	61.4	56.4	61.9	0.29
Smoking [%]	73.8	63.4	49.8	0.00001 # * &
Diabetes mellitus [%]	8.5	20.2	67.5	0.00001 # * &
Past myocardial infarction [%]	19.1	18.2	19.0	0.96
Mean blood glucose on admission [mmol/l (mg/dl)]	6.4±0.99 (115.2 ±17.8)	9.2±0.89 (165.6±16.0)	15.8±4.5 (284.4±81.0)	0.00001 # * &
Mean red cell count [M/mm ³]	4.5±0.49	4.6±0.48	4.5±0.51	0.43
Mean haemoglobin concentration [mmol/l]	9.0±1.0	8.9±1.2	8.8±1.2	0.22
Mean chest pain duration [h]	5.2±4.2	4.4±3.0	5.3±4.8	0.016 *
Anterior wall myocardial infarction [%]	38.6	39.7	38.7	0.94
Fibrinolysis prior to PCI [%]	24.4	29.3	33.9	0.023 * &
Cardiogenic shock [%]	4.5	7.5	20.2	0.00001 * &

– $p < 0.05$ for group I vs. group II, * – $p < 0.05$ for group II vs. group III, & – $p < 0.05$ for group I vs. group III

$p < 0.05$ (two-sided). Statistical analyses and all calculations were performed using Statistica PL software v. 6.0 (StatSoft Inc.).

Results

A total of 1027 consecutive patients with STEMI treated with PCI were enrolled. The incidence of diabetes in the entire study population was 26.1% and cardiogenic shock – 9.2%. Number of patients in the individual groups was as follows: group I – 472 subjects, group II – 307 subjects, and group III – 248 subjects. Patients with elevated BG on admission were older, more often females, more frequently presented with hypertension and diabetes, and less frequently were smokers. Higher rates of fibrinolytic therapy prior to PCI and cardiogenic shock were also found in this group. Clinical characteristics of studied groups are shown in Table I.

Coronary angiography performed in the group of patients with elevated BG on admission showed significantly higher rate of multi-vessel disease and baseline TIMI 0-1 than in the normoglycaemic patients (63.8 vs. 69.1 vs. 73.8%). A strong trend to a higher rate of reocclusion in patients with elevated BG on admission was also observed. Angiographic characteristics are summarised in Table II.

Patients with elevated BG on admission had higher levels of myocardial necrosis enzymes and lower left

ventricular ejection fraction (LVEF). Increased BG on admission was also related to a higher rate of in-hospital stroke events. In-hospital mortality was 2 and 5 times higher in groups II and III, respectively, compared to group I; a similar relationship was maintained during a 12-month follow-up. The Kaplan-Meier survival curves are shown in Figure 1. Moreover, higher rates of stroke and major adverse cardiovascular events (MACE), defined as total incidence of stroke, re-infarction and death, were observed in patients with elevated BG on admission. The details of in-hospital and 12-month follow-up are presented in Table III.

Multivariate analysis showed that BG on admission was a predictor of an increased 12-month mortality, independently from cardiogenic shock, multi-vessel coronary artery disease, hypertension and age. Hazard ratio for each 1 mmol/l (18 mg/dl) of BG increase was 1.06 (95% CI 1.02-1.09). Figure 2 depicts the relationship between BG on admission and 12-month mortality. Diabetes had no influence on 12-month mortality. Results of the multivariate analysis are depicted in Figure 3.

Discussion

This study showed that increased baseline BG was an independent predictor of adverse outcome in patients with acute MI treated with primary PCI.

Table II. Angiographic characteristics of the studied patients

Parameters	Group I	Group II	Group III	p
Angiographic location of infarction [%]				
RCA	40.0	46.6	46.8	NS
CX	17.0	12.1	10.9	NS
LAD	40.3	39.4	40.3	NS
LM	0.4	0.7	0.8	NS
Baseline TIMI 0-1 [%]	63.8	69.1	73.8	0.02 # &
Final TIMI 3 [%]	91.5	89.3	87.9	NS
Multi-vessel coronary artery disease [%]	48.5	55.1	64.1	0.0003 * &
Stenting [%]	63.1	65.5	66.9	NS
Re-occlusion [%]	4.5	6.8	8.9	0.057

Abbreviations: RCA – right coronary artery, Cx – circumflex branch of the left coronary artery, LAD – left anterior descending coronary artery, LM – left main coronary artery, TIMI – Thrombolysis in Myocardial Infarction

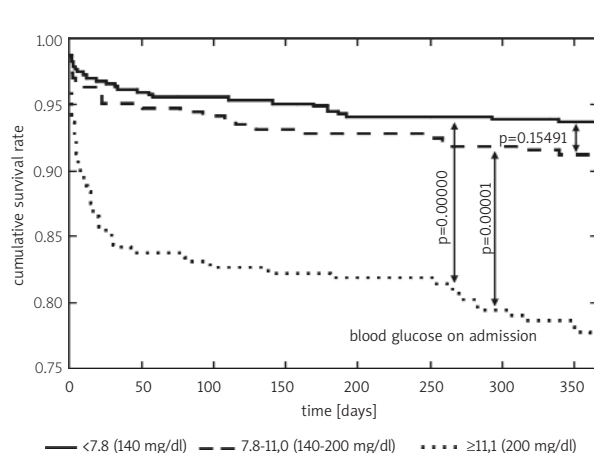
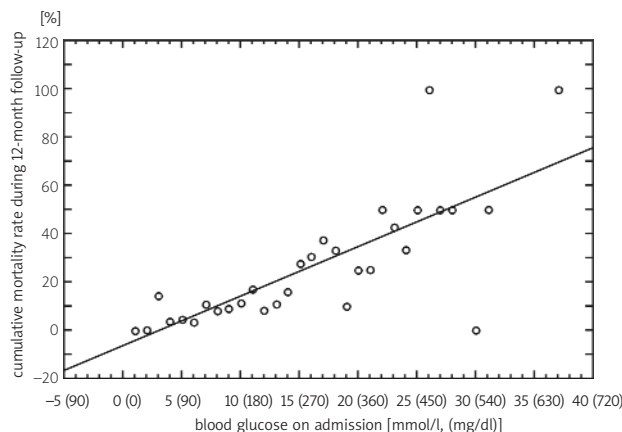
– $p < 0.05$ for group I vs. group II, * – $p < 0.05$ for group II vs. group III, & – $p < 0.05$ for group I vs. group III

Table III. Characteristics of in-hospital and 12-month follow-up of the studied patients

Parameters	Group I	Group II	Group III	p
Max creatine kinase level [IU/l]	2044.6±1655.1	2441.9±1861.5	2882.3±2747.4	0.00001
Left ventricular ejection fraction [%]	46.1±8.0	44.3±8.5	42.2±9.0	0.00001 # &
Gastrointestinal bleeding [%]	1.7	0.7	3.2	0.072*
PCI-related haematoma [%]	3.0	3.9	6.1	NS
Transfusion of packed red blood cells [%]	3.4	4.6	7.7	0.037
Urgent CABG [%]	1.6	2.8	0.4	NS
In-hospital stroke [%]	1.1	1.3	4.4	0.0049
In-hospital mortality [%]	2.8	4.9	13.3	0.00001 * &
Mean hospitalisation duration [days]	8.5±4.8	8.5±4.9	9.3±6.1	NS
Stroke during 12-month follow-up [%]	1.3	2.9	6.9	0.022 &
Reinfarction during 12-month follow-up [%]	5.1	5.2	4.8	NS
A 12-month mortality [%]	6.4	9.1	22.6	0.00001 * &
MACE during 12-month follow-up [%]	14.0	17.6	31.1	0.00001 # * &

Abbreviations: PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting, MACE – major adverse cardiac events

– $p < 0.05$ for group I vs. group II, * – $p < 0.05$ for group II vs. group III, & – $p < 0.05$ for group I vs. group III

**Figure 1.** Cumulative survival rate (Kaplan-Meier method) – 12-month follow-up**Figure 2.** 12-month mortality rate according to blood glucose on admission

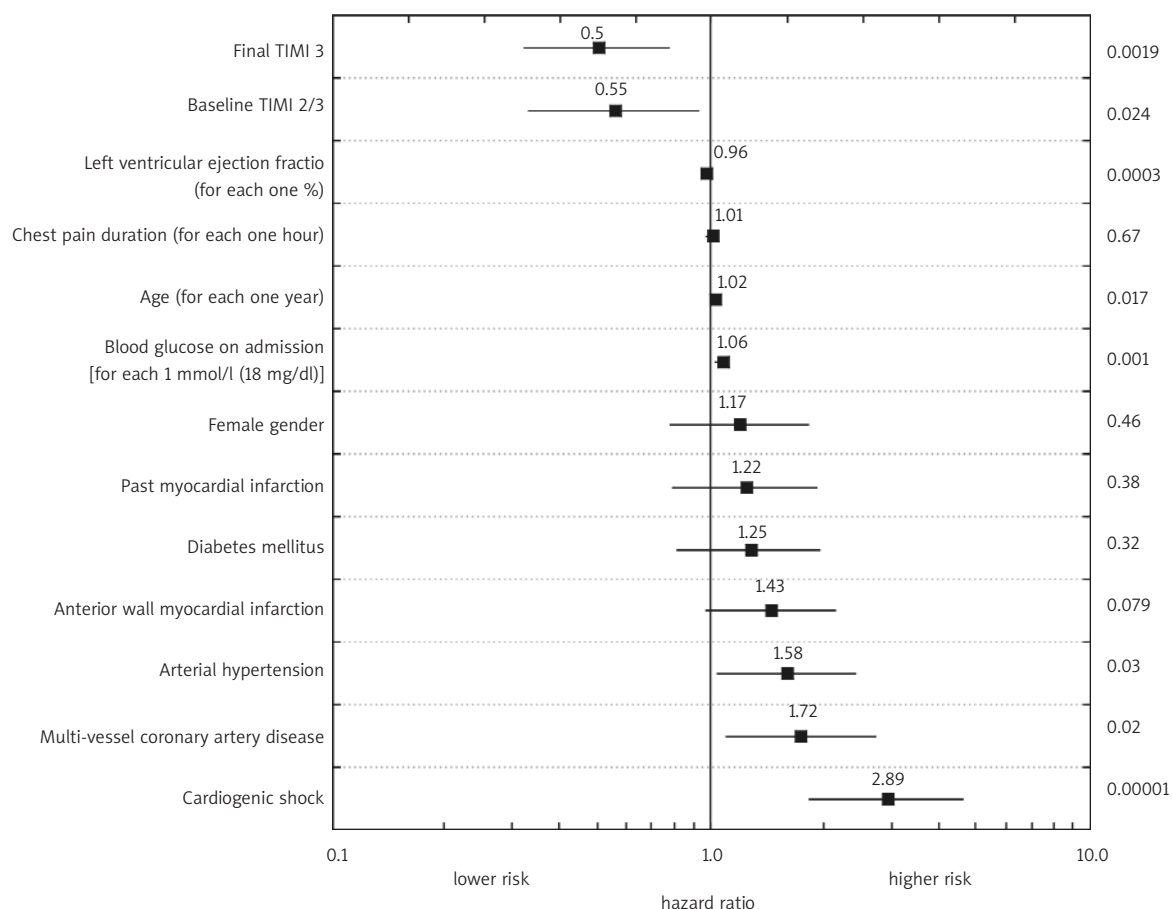


Figure 3. Factors affecting 12-month survival. The hazard ratio and 95% confidence intervals are presented

Having in mind the large variety of selection criteria seen in other studies, we selected analysed groups on the basis of BG levels as borderline for diagnosis of intolerance of glucose and diabetes mellitus when performing oral glucose tolerance test [18]. Such a distinction allowed indication of differences in clinical characteristics and treatment outcomes in our study.

It is worth mentioning that clinical and angiographic characteristics of patients with MI depend on BG on admission. The relationship between increased BG in acute MI and age, female gender, presence of arterial hypertension and lower number of smokers has also been showed by other authors [9, 13, 14].

Our study showed that in patients with BG ≥ 11.1 mmol/l (200 mg/dl) cardiogenic shock was diagnosed 4.5 times more frequently than in subjects with BG < 7.8 mmol/l (140 mg/dl). This finding is important because cardiogenic shock was the most powerful predictor of increased 12-month mortality. Moreover, a high percentage of diabetes (67.5%)

was noted in patients with baseline BG ≥ 11.1 mmol/l (200 mg/dl). A lower diabetes rate (42.0%) was reported in a similar group by Straumann et al. [13], whereas Ishihara et al. found diabetes in 61.0% of patients with BG > 11.0 mmol/l [14].

It should be stressed that admission BG ≥ 11.1 mmol/l (200 mg/dl) in patients without prior diabetes does not unequivocally indicate diabetes mellitus. Despite measuring BG ≥ 11.1 mmol/l (200 mg/dl) diagnosis of diabetes requires evidence of increased BG typical of diabetes after the acute phase of MI. Tenerz et al. reported that diabetes developed during long-term follow-up only in 50% of patients without prior diabetes and BG ≥ 11.1 mmol/l at the onset of MI [19]. It has also been shown that BG during the acute phase of MI may be related to the baseline culprit artery blood flow. Timmer et al. provided evidence that hyperglycaemia (≥ 7.8 mmol/l) on admission was an independent predictor of baseline TIMI grade 0-2 flow [20]. In our study a correlation between increased BG and

worsened baseline coronary blood flow was seen in all three analysed groups.

In our study elevated BG in the acute phase of MI was also associated with the presence of a multi-vessel coronary artery disease. However, this finding was not reported by other investigators. Ishihara et al. reported that multi-vessel coronary artery disease was present in 26% and 22% of patients with or without hyperglycaemia, respectively (NS) [15]. These divergent outcomes may result from a low percentage of diabetes in patients with hyperglycaemia; however, it has been documented that the presence of diabetes is associated with multi-vessel coronary artery disease [3, 21].

Interestingly, published data indicate that epicardial arterial blood flow after PCI is not associated with the of admission BG [13, 15]. Effectiveness of angioplasty in our study was 90.0%, and no statistically significant difference was revealed with respect to epicardial blood flow between the analysed groups.

It has been shown that elevated BG in acute MI patients was associated with higher levels of myocardial necrosis enzymes and lowers LVEF [8, 11, 13-16]. Ishihara et al. reported that LVEF decreased along with increased BG levels on admission [15]. A similar correlation was shown in our study. Ejection fraction in patients with BG ≥ 11.1 mmol/l (200 mg/dl) was about 4% lower than in patients with BG < 7.8 mmol/l (140 mg/dl). Significantly more frequent transfusion of packed red cells in patients with higher BG may also be associated with the trend towards higher incidence of gastrointestinal bleeding in these groups of patients. This may result from a higher incidence of fibrinolytic treatment prior to PCI. However, mean haemoglobin concentration and the mean red blood cell count on admission were comparable.

Various clinical and angiographic characteristics of patients with elevated BG on admission are reflected by worse prognosis. Wahab et al. conducted a very interesting analysis dividing patients into four groups depending on BG on admission and the presence of diabetes. Hyperglycaemic (> 11.0 mmol/l) and non-diabetic patients had significantly higher in-hospital and 12-month mortality rate compared to diabetic patients without hyperglycaemia [22]. Similarly, a higher 6-month mortality in non-diabetic patients with hyperglycaemia was documented by Ainla et al. [23]. These relationships might suggest that BG level in acute phase of MI has a more pronounced effect on patient mortality than the presence of diabetes per se. Additionally, Iwakura et al. reported that, in contrast to

diabetes, BG on admission was an independent predictor of the no-reflow phenomenon [16], which is associated with considerably higher mortality [14].

In our study, elevated BG level on admission was associated with an increased in-hospital and 12-month mortality. Multivariable analysis showed that for each 1 mmol/l (18 mg/dl) increase of glucose concentration on admission, hazard ratio increased by 6% during a 12-month follow-up, whereas the presence of diabetes did not affect mortality. Ishihara et al. showed a higher in-hospital mortality rate in patients hyperglycaemic at baseline. In-hospital mortality in diabetic and non-diabetic patients was comparable. However, for each 1 mmol/l of baseline BG increase on admission, hazard ratio of in-hospital death was 1.10 (95% CI 1.05-1.15) higher [14]. Straumann et al. reported that 30-day and 3- and 7-year mortality rates were dependent on BG measured in acute phase of MI. Three- and 7-year mortality was 7.1%, 9.8% and 26.6% in patients with BG < 7.8 mmol/l, 7.8-11.0 mmol/l, and > 11.0 mmol/l, respectively. Multivariable analysis showed admission BG to be an independent predictor of mortality, but not of the presence of diabetes [13].

The results of our study not only confirm the role of established risk factors having an effect on 12-month mortality, but also suggest that BG on admission may identify patients with adverse prognosis. One of the most important findings is the fact that BG on admission in patients with acute MI treated with PCI may be of a higher prognostic value than the presence of diabetes per se.

Conclusion

Elevated blood glucose concentration in the acute phase of STEMI treated with PCI is a potent predictor of adverse prognosis.

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Związek pomiędzy poziomem glikemii przy przyjęciu a rokowaniem wewnątrzszpitalnym i jednorocznym chorych z zawałem serca leczonych przezskórną interwencją wieńcową

Mariusz Gąsior¹, Gabriela Stasik-Pres¹, Damian Pres¹, Piotr Lech¹, Marek Gierlotka¹, Andrzej Lekston¹, Michał Hawranek¹, Mateusz Tajstra¹, Zbigniew Kalarus², Lech Poloński¹

¹ III Katedra i Oddział Kliniczny Kardiologii, Śląski Uniwersytet Medyczny, Śląskie Centrum Chorób Serca, Zabrze

² I Katedra i Oddział Kliniczny Kardiologii, Śląski Uniwersytet Medyczny, Śląskie Centrum Chorób Serca, Zabrze

Streszczenie

Wstęp: Występowanie cukrzycy u chorych z zawałem serca zwiększa śmiertelność wewnątrzszpitalną i odległą. Istnieją doniesienia, że poziom glikemii w ostrej fazie zawału może determinować rokowanie chorych. Niewiele jest publikacji, w których badano zależność pomiędzy poziomem glikemii przy przyjęciu a rokowaniem chorych z zawałem serca bez względu na obecność cukrzycy.

Cel: Określenie wpływu poziomu glikemii przy przyjęciu na rokowanie wewnątrzszpitalne i jednoroczne chorych z zawałem serca z uniesieniem odcinka ST (STEMI) leczonych za pomocą przezskórnej interwencji wieńcowej (PCI).

Metodyka: Analizie poddano kolejnych chorych z ostrym STEMI leczonych za pomocą PCI. Do badania włączono także chorych z zawałem serca powikłanym wstrząsem kardiogennym. Przeptyw w tętnicy nasierdziejowej oceniano wg skali TIMI (*Thrombolysis in Myocardial Infarction*). Skuteczny zabieg PCI definiowano jako uzyskanie przeptywu TIMI 3 i obecność rezydualnej stenozы ≤30% bez cech dyssekcji ograniczającej przeptyw przez tętnicę. Na potrzeby niniejszej analizy chorych podzielono na trzy grupy w zależności od poziomu glikemii przy przyjęciu. Grupę pierwszą stanowili chorzy z poziomem glikemii przy przyjęciu <7,8 mmol/l (140 mg/dl), grupę drugą chorzy z poziomem glikemii 7,8–11,1 mmol/l (140–200 mg/dl), grupę trzecią chorzy z poziomem glikemii ≥11,1 mmol/l (200 mg/dl).

Wyniki: Do badania zakwalifikowano 1027 kolejnych chorych ze STEMI leczonych PCI. Odsetek występowania cukrzycy w całej analizowanej grupie wynosił 26,1%, natomiast wstrząsu kardiogennego – 9,2%. Liczebność poszczególnych grup była następująca: grupa pierwsza – 472 chorych, grupa druga – 307 chorych, grupa trzecia – 248 chorych. Chorzy z wyższym poziomem glikemii przy przyjęciu byli starsi, częściej płci żeńskiej, częściej występowały u nich nadciśnienie tętnicze i cukrzyca, rzadziej palili papierosy. Stwierdzono także wyższy odsetek stosowanego leczenia fibrynolitycznego przed PCI oraz wstrząsu kardiogennego (4,5 vs 7,5 vs 20,2%). W wykonanej koronarografii w grupie chorych z wyższym poziomem glikemii przy przyjęciu stwierdzono istotnie częściej wielonaczyniową chorobę wieńcową oraz wyższy odsetek wyjściowego przeptywu TIMI 0–1 (63,8 vs 69,1 vs 73,8%). Chorzy z wyższym poziomem glikemii przy przyjęciu charakteryzowali się większym stężeniem enzymów martwiczych mięśnia sercowego oraz niższą frakcją wyrzutową lewej komory. Wyższy poziom glikemii przy przyjęciu związany był także z wyższym odsetkiem występowania udaru mózgu w okresie wewnątrzszpitalnym (1,1 vs 1,3 vs 4,4%). Zaobserwowano, że śmiertelność wewnątrzszpitalna jest ok. 2-krotnie [w grupie z poziomem glikemii 7,8–11,1 mmol/l (140–200 mg/dl)] i około 5-krotnie [w grupie z poziomem glikemii ≥11,1 mmol/l (200 mg/dl)] wyższa w stosunku do grupy chorych z glikemią <7,8 mmol/l (140 mg/dl). Podobna zależność utrzymała się w obserwacji jednorocznej. Śmiertelność jednoroczna była zależna od poziomu glikemii w ostrej fazie zawału i wynosiła 6,4 vs 9,1 vs 22,6% odpowiednio dla chorych z glikemią <7,8 mmol/l (140 mg/dl); w przedziale 7,8–11,1 mmol/l (140–200 mg/dl) i ≥11,1 mmol/l (200 mg/dl). Ponadto, stwierdzono częstsze występowanie udaru mózgu i MACE (*Major Adverse Cardiovascular Events*). W przeprowadzonej analizie wieloczynnikowej wykazano, że niezależnym czynnikiem determinującym wyższą śmiertelność jednoroczną był poziom glikemii przy przyjęciu. Na każdy 1 mmol/l (18 mg/dl) glikemii względne ryzyko zgonu wynosiło HR=1,06 (95% CI 1,02–1,09). Istotne jest, iż obecność cukrzycy nie miała wpływu na śmiertelność jednoroczną.

Wniosek: Wyższy poziom glikemii w ostrej fazie STEMI leczonego za pomocą PCI jest silnym predyktorem gorszego rokowania.

Słowa kluczowe: zawał serca, cukrzyca, poziom glikemii przy przyjęciu

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Adres do korespondencji:

dr hab. n. med. Mariusz Gąsior, III Katedra i Oddział Kliniczny Kardiologii, ŚUM, Śląskie Centrum Chorób Serca, ul. Szpitalna 2, 41-800 Zabrze, tel.: +48 32 273 23 16, e-mail: mariuszgasion@poczta.onet.pl

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