

# Impact of Reactive Hyperglycaemia on Length of Hospitalisation and Prognosis in Patients with Acute ST Segment Elevation Myocardial Infarction

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## ABSTRACT

**Aim:** Disturbance of carbohydrate metabolism in the course of acute myocardial infarction is a known factor worsening cardiovascular prognosis. Aim of this study was to assess an impact of reactive hyperglycaemia on length of hospitalisation and prognosis in patients with acute myocardial infarction treated with primary percutaneous coronary intervention.

**Methods:** 92 patients with acute ST segment elevation myocardial infarction qualified for primary percutaneous coronary intervention were included. The study population was divided into groups regarding glucose level on admission (reactive hyperglycaemia) or concentration of HbA1c as follows: group with higher level of glycaemia on admission (Glc  $\geq 7,8$  mmol/L, n=46), group with lower level of glycaemia on admission (Glc  $< 7,8$  mmol/L, n=46), group with lower concentration of HbA1c ( $< 6,5\%$ , n=71) and higher concentration of HbA1c ( $\geq 6,5\%$ , n=21). Long and short term prognosis was assessed on the basis of incidence of major adverse cardiovascular events (MACE) in the course of hospital stay, 4 – month and 4 – year follow – up.

**Results:** Amongst patients with Glc  $\geq 7,8$  mmol/L there was significantly higher level of CK and CK-MB assessed during first 48 hours of hospitalisation (CK p=0,034, CK-MB p=0,01, respectively), significantly higher level of leukocytes (p $< 0,001$ ) and length of hospital stay (p=0,028). During 4 year follow up, group of patients with higher glucose level on admission had significantly higher incidence of MACE (p=0,01) and higher

incidence of diabetes mellitus (p=0,011). During 4 year follow up observation higher incidence of DM was observed in group of patients with HbA1c  $\geq 6,5\%$ .

**Conclusions:** Group of patients with disturbances of carbohydrate metabolism had inferior clinical course. Length of hospitalisation was longer and long term observation revealed higher incidence of cardio – vascular complications. Probability of diagnosis of diabetes mellitus in long-term observation was higher among group of patients with elevated values of glycaemia on admission and higher concentration of glycated haemoglobin during hospitalisation in the course of STEMI.

**Keywords:** Reactive Hyperglycaemia, Acute Myocardial Infarction.


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## INTRODUCTION

Continuous progress in medicine systematically leads to better results of treatment of patients with myocardial infarction. Unfortunately patients with acute ST segment elevation myocardial infarction and concomitant diabetes have worse prognosis, despite reduction of intrahospital and long term mortality comparing to previous years.<sup>1-4</sup> Moreover available literature points out, that most urgent patients hospitalized in a cardiological unit develop reactive hyperglycemia.<sup>5,6</sup>

However, this is partly due to concomitant diabetes mellitus. Among high percentage of patients, disturbances of carbohydrate metabolism are diagnosed only within hospitalisation.<sup>7,8</sup> Available literature reports, that every sixth patient hospitalised due to acute myocardial infarction is additionally diagnosed with undiscovered diabetes, but amongst them two out of five patients did not have diabetes diagnosed directly after admission, but 6 months or even more after myocardial infarction.<sup>9</sup> Consequences of undiagnosed

disease constitutes delayed treatment and earlier development of chronic complications of diabetes.<sup>10</sup> Aim of this study was to assess impact of reactive hyperglycaemia on length of hospitalisation and prognosis in patients diagnosed with acute ST segment elevation myocardial infarction treated with primary percutaneous coronary angioplasty. Additional assessment included probability of development of diabetes in long term observation among patients with disturbed carbohydrate metabolism diagnosed in the course of acute myocardial infarction.

## METHODS

### Study Population

Present paper is a prospective study accomplished in 2014 – 2016 years in John Paul II Hospital in Kraków, Poland.

Study population comprised of 165 patients with the first time ST segment elevation myocardial infarction in electrocardiographic examination, defined as new, lasting at least 30 minutes ST segment elevation measured at point J in at least two adjacent leads and cut – off point on the level of  $\geq 1$  mm in every lead except of V2 and V3, in which cut – off point was determined as  $\geq 2$  mm in men  $\geq 40$  years old and  $\geq 1,5$  in women and qualified for urgent primary percutaneous coronary intervention (pPCI). Exclusion criteria included previously diagnosed diabetes (prior to hospital admission), signs of heart failure (III or IV degree according to Killip – Kimball scale), necessity of intravenous amines or glucose solution intake on admission, prior myocardial infarction, coronary artery bypass graft surgery, sudden cardiac arrest in the past or at current hospitalisation, prior fibrinolytic treatment, cancer or autoimmune disease, liver failure (ALAT level  $> 1,5x$  upper limit of normal) and renal failure (GFR  $< 30$  ml/min/1,73 m<sup>2</sup>) assessed during lab tests performed in Emergency Room and lack of complete diagnostics of carbohydrate metabolism during hospitalisation.

Finally, 92 patients were included in the present study and following tests were performed:

### Laboratory Assessment

- A. Glucose level on admission and fasting glucose level on the following day measured in venous blood serum via enzymatic method with hexokinase, UV test, Olympus AU560 apparatus manufactured by Biomerieux,
- B. Glucose tolerance test with 75 grams of glucose intake and glycaemia assessed in venous blood serum in the fasted state and 2 hours after glucose intake. Test performed on the day of discharge (often on 4<sup>th</sup>-5<sup>th</sup> day of hospitalisation).

Criteria of glucose metabolism state were defined according to WHO<sup>1</sup> as follows:

1. **Normal glucose regulation** = 3,9 – 5,5 mmol/L (70-99 mg/dL)
2. **Impaired fasting glucose** = 5,6 – 6,9 mmol/L (100-125 mg/dL)
3. **Impaired glucose tolerance** = 7,8 – 11 mmol/L (140-199 mg/dL) measured in 120 minute of glucose tolerance test
4. **Prediabetes** = Impaired fasting glucose and/or impaired glucose tolerance
5. **Diabetes**
  - a) casual glycaemia  $\geq 11,1$  mmol/L ( $\geq 200$  mg/dL) with concomitant signs of hyperglycaemia,

- b) fasting glucose  $\geq 7,0$  mmol/L ( $\geq 126$  mg/dL) assessed twice,
- c) glycaemia  $\geq 11,1$  mmol/L ( $\geq 200$  mg/dL) in 120 minute of glucose tolerance test.

- C. Concentration of glycated haemoglobin (HbA1c) from capillary blood was assessed by high performance liquid chromatography (HPLC), Variant apparatus manufactured by BioRad, using analytic method certified by National Glycohemoglobin Standardization Program,
- D. Damage level of myocardium was assessed on the basis of concentration of cardiac markers such as creatinine kinase (CK), fraction MB of creatinine kinase (CKMB) in 0, 90 minute and then 8, 16, 24, and 48 hours after patient's admission to the hospital.
- E. Assessment of inflammatory markers: leukocytosis (flow cytometry method using laser apparatus Sysmex XT) and hs-CRP (high sensitivity immunoturbidimetric method using Cobas C501 apparatus, Roche company),
- F. Assessment of renal parameters: creatinine (assessed by color kinetic test, Jaffe method using Cobas C501 apparatus, Roche company) and eGFR (glomerular filtration rate calculated according to MDRD equation).

### Echocardiographic Assessment

Complete echocardiography examination was performed during hospitalization after coronary angioplasty and at 4 months after discharge follow up visit, using the GE Vivid 3 Pro (GE Healthcare, US), equipped with a multifrequency harmonic transducer (2.5–4 MHz). Systolic function of the left ventricle was estimated with LVEF by means of the Simpson method. The average values of 3 consecutive measurements were recorded.

### Angiographic Assessment

Examination was performed using Axiom Artis dFC SIEMENS equipment. Angiographic recordings involved at least three heart beat loops to the disappearance of contrast in coronary arteries. Left coronary artery was evaluated in four standard viewing angles (LAO 50/CRAN 20), RAO 30/CAUD 20, LAO 40/CAUD 40, AP CRAN 30), right coronary artery in two viewing angles (LAO 40, RAO 40). Recordings were anonymized and assessed by two experienced operators. The analysis covered target lesion, thrombectomy, collateral circulation to occlusive coronary artery (Rentrop scale) and other visible atherosclerotic lesions in coronary arteries. Contrast flow in target vessel was assessed in semi-quantitative TIMI scale before and after primary coronary intervention (pPCI). Study population was divided in two groups, regarding glucose concentration level on admission (reactive hyperglycaemia) or HbA1c concentration. Group with higher glucose level on admission (Glc  $\geq 7,8$  mmol/L, n=46) and group with lower level of glucose on admission (Glc  $< 7,8$  mmol/L, n=46) and group with lower HbA1c ( $< 6,5\%$ , n=71), group with higher concentration of HbA1c ( $\geq 6,5\%$ , n=21).

### STUDY END – POINTS

#### Primary End – Points

1. Length of hospitalization as equivalent of prognosis during hospital stay.
2. Short and long term prognosis as complex end – point evaluated on the basis of frequency of adverse

cardiovascular events (MACE: death, myocardial infarction, stroke, heart failure requiring hospitalization and renewed revascularization).

**Secondary End – Points**

1. Extensity of acute myocardial infarction evaluated on the basis of cardiac markers dynamics and echocardiographic findings.
2. Level of disturbances of glucose metabolism among hospitalized patients at 4 month and 4-year follow-up observation.

**Ethical Issues:** The study protocol complied with the Declaration of Helsinki and was approved by the Ethics Committee of Jagiellonian University (no. KBET/120/B/2007 to JZ). Each study participant provided written informed consent before enrollment.

**Statistical Analysis:** Quantitative traits were characterized by specifying the mean and standard deviation with 95% confidence interval for mean, median with quartile distribution and maximum and minimum value. Qualitative traits were characterized by numerical and percentage distribution. The average values of quantitative traits were compared using Student's t test for independent traits if all test assumptions were met. In case of abnormal distribution of at least one trait in investigated group nonparametric Mann-Whitney test was used. However, in the absence of homogeneity of variance of the examined feature in populations, the Welch test was used. Comparisons of the average values of the quantitative traits in a larger number of patients were based on a one-way ANOVA analysis of variance using the Kruskal-Wallis test (in the case of non-compliance of the distribution of the trait with the normal distribution) or by the Welch test (in the absence of homogeneity of variance). The compliance of the empirical distribution of the quantitative trait with the theoretical normal distribution was checked by the Shapiro-Wilk test. The homogeneity of the quantitative trait variance in several populations was checked by Levene's test. The assessment of changes in quantitative trait over time was carried out on the basis of a two-factor analysis of variance with repeated measurements or a polynomial analysis of variance - when the assumption of sphericity (verified by Mauchley's test) was not met. The relationship of two quantitative features was assessed using the Pearson linear correlation coefficient or in the case of non-compliance of the distribution of at least one of the examined features with the normal distribution - using the Spearman rank correlation factor. However, the relationship of the two qualitative features was verified based on the chi-square test or Fisher's exact test if the expected numbers were insufficient. The results were considered statistically significant if the calculated probability level did not exceed the significance level  $\alpha = 0.05$ . Statistical calculations were made using R software (version 3.1.2).

**RESULTS**

Table 1 presents patients clinical characteristic, taking into account differences between groups regarding glucose level on admission and concentration of HbA1c. When assessing routine laboratory tests during first days of hospitalization, leukocytes level differed significantly between patients with glycaemia on admission lower than 7,8 mmol/L and equal or higher than 7,8 mmol/L ( $p < 0,001$ ), (Fig. 1a). There was not any statistically significant difference between groups regarding other inflammatory marker (hs-CRP,  $p = 0,081$ ). (Fig. 1b).

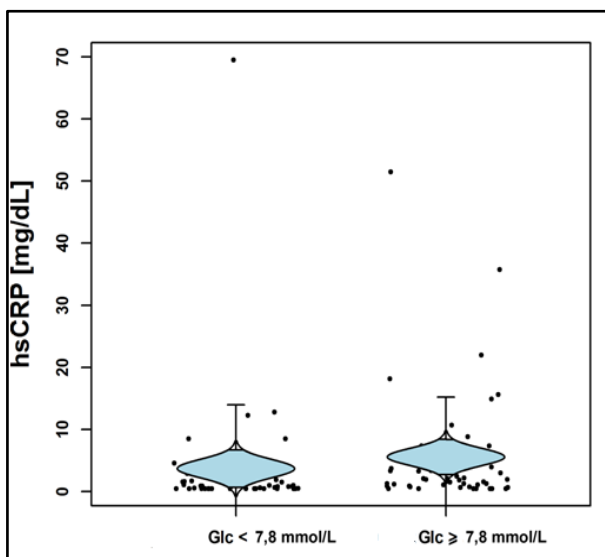
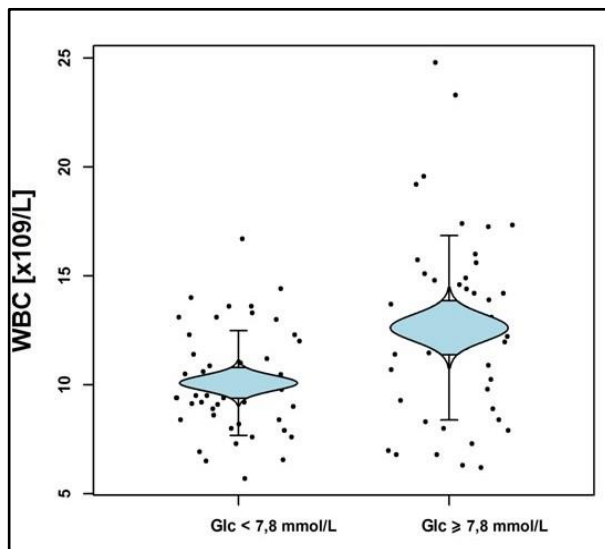


Figure 1 (a & b): Comparison of inflammatory parameters in the blood (WBC [x109 / l];  $p < 0.001$  (Fig. 1a) and hs-CRP [mg / dl];  $p = 0.081$ , ( Fig. 1b) of patients treated with PCI in STEMI depending on the blood glucose level on admission.

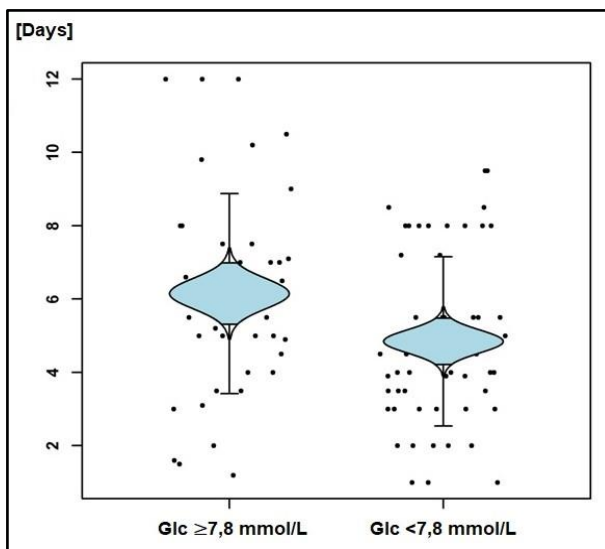


Figure 2: Average length of hospitalization [days] of patients treated with pPCI in the acute phase of myocardial infarction depending on the blood glucose level on admission ( $p = 0.028$ ).

**Table 1: Clinical characteristics of patients treated with PCI in STEMI depending on the blood glucose level on admission and HbA1c concentration.**

|                                   | Number (n) | Glc on admission 7.8 mmol/l | Present    | p value | Number (n) | HbA1c 6.5% | Present       | p value |
|-----------------------------------|------------|-----------------------------|------------|---------|------------|------------|---------------|---------|
| Age ≥65 years                     | 46         | <                           | 25 (54.3%) | 0.164   | 71         | <          | 55.71 - 60.94 | 0,004   |
|                                   | 46         | ≥                           | 29 (63.2%) |         | 21         | ≥          | 61.65 – 71.01 |         |
| Male gender                       | 46         | <                           | 23 (50.0%) | 0.582   | 71         | <          | 76 (82.6%)    | 0.377   |
|                                   | 46         | ≥                           | 24 (52.2%) |         | 21         | ≥          | 16 (17.4%)    |         |
| Arterial hypertension             | 46         | <                           | 22 (47.8%) | 0.296   | 71         | <          | 36 (50.7%)    | 0.366   |
|                                   | 46         | ≥                           | 27 (58.7%) |         | 21         | ≥          | 13 (61.9%)    |         |
| Lipid metabolism disorders        | 46         | <                           | 28 (60.9%) | 0.832   | 71         | <          | 42 (59.2%)    | 0.821   |
|                                   | 46         | ≥                           | 27 (58.7%) |         | 21         | ≥          | 13 (61.9%)    |         |
| BMI ≥30,0                         | 46         | <                           | 8 (17.4%)  | 0.343   | 71         | <          | 25 (35.2%)    | 0.019   |
|                                   | 46         | ≥                           | 11 (23.1%) |         | 21         | ≥          | 12 (57.1%)    |         |
| Tobacco addiction                 | 46         | <                           | 30 (65.2%) | 0.204   | 71         | <          | 45 (63.4%)    | 0.093   |
|                                   | 46         | ≥                           | 24 (52.2%) |         | 21         | ≥          | 9 (42.9%)     |         |
| CAD at family history             | 46         | <                           | 14 (30.4%) | 0.482   | 71         | <          | 20 (28.2%)    | 0.693   |
|                                   | 46         | ≥                           | 11 (23.9%) |         | 21         | ≥          | 5 (23.8%)     |         |
| Kidney diseases                   | 46         | <                           | 2 (4.3%)   | –       | 71         | <          | 2 (2.8%)      | –       |
|                                   | 46         | ≥                           | 3 (6.5%)   |         | 21         | ≥          | 3(14.2%)      |         |
| Thyroid diseases                  | 46         | <                           | 4(8.7%)    | –       | 71         | <          | 6 (8.5%)      | –       |
|                                   | 46         | ≥                           | 4 (8.7%)   |         | 21         | ≥          | 2 (9.5%)      |         |
| A history of CAD                  | 46         | <                           | 12 (26.1%) | 0.203   | 71         | <          | 14 (19.7%)    | 0.313   |
|                                   | 46         | ≥                           | 9 (19.6%)  |         | 21         | ≥          | 7 (33.3%)     |         |
| State after myocardial infarction | 46         | <                           | 2 (4.3%)   | 0.456   | 71         | <          | 6 (8.5%)      | 0.330   |
|                                   | 6          | ≥                           | 5 (10.9%)  |         | 21         | ≥          | 1 (4,8%)      |         |

**Table 2: Analysis of the state of carbohydrate metabolism of patients treated with PCI in STEMI during hospitalization depending on the blood glucose level on admission and HbA1c concentration (NGR = Normal glucose regulation, IFG = Impaired fasting glucose, IGT = Impaired glucose tolerance, DM = type 2 diabetes mellitus).**

|                  | Number (n)  | Glucose metabolism state |           |            |            | p value |
|------------------|-------------|--------------------------|-----------|------------|------------|---------|
|                  |             | NGR                      | IFG       | IGT        | DM de novo |         |
| Glc on admission | 46          | 24 (52,2%)               | 5 (10,9%) | 13 (28,3%) | 4 (8,7%)   | 0.015   |
|                  | <7,8 mmol/l |                          |           |            |            |         |
|                  | 46          | 17 (37%)                 | 5 (10,9%) | 9 (19,6%)  | 15 (32,6%) |         |
|                  | ≥7,8 mmol/l |                          |           |            |            |         |
| HbA1c            | 71          |                          |           |            |            |         |
|                  | <6,5%       | 36 (50,7%)               | 8 (11,3%) | 17 (23,9%) | 10 (14,1%) |         |
|                  | ≥6,5%       | 5 (23,8%)                | 2 (9,5%)  | 5 (23,8%)  | 9 (42,9%)  | 0.027   |

**Table 3: Incidence of adverse cardiovascular events in the 4-month and 4-year follow-ups of pPCI-treated patients with STEMI depending on the blood glucose level on admission.**

| Glc on admission           | <7.8 mmol/L    |    | ≥7.8 mmol/L |        | <7.8 mmol/L   |    | ≥7.8 mmol/L |      | p value |
|----------------------------|----------------|----|-------------|--------|---------------|----|-------------|------|---------|
|                            | after 4 months |    | p value     |        | after 4 years |    | p value     |      |         |
| <b>MACE</b>                |                |    |             |        |               |    |             |      |         |
| In Total                   | 3 (6.9%)       | vs | 9 (24.3%)   | 0.0633 | 11 (23.9%)    | vs | 23 (50%)    | 0.01 |         |
| Death                      | 1 (2.1%)       | vs | 1 (2.1%)    |        | 2 (4.3%)      | vs | 4 (8.7%)    |      |         |
| Cardiac death              | 0              | vs | 1 (2.1%)    |        | 1 (2.1%)      | vs | 2 (4.3%)    |      |         |
| Myocardial infarction      | 0              | vs | 2 (4.3%)    |        | 3 (6.5%)      | vs | 8 (7.4%)    |      |         |
| PCI/CABG                   | 1 (2.1%)       | vs | 4 (8.7%)    |        | 4 (8.7%)      | vs | 9 (9.6%)    |      |         |
| Hospitalisation due to CHF | 1 (2.1%)       | vs | 2 (4.3%)    |        | 1 (2.1%)      | vs | 2 (4.3%)    |      |         |
| Stroke                     |                |    | 0           |        | 1 (2.1%)      | vs | 0           |      |         |
| Diabetes Mellitus          |                |    |             |        | 6 (13,0%)     | vs | 14 (30,4%)  |      | 0,011   |

**Table 4: Incidence of adverse cardiovascular events in the 4-month and 4-year follow-ups of pPCI-treated patients with STEMI depending on HbA1c concentration.**

| HbA1c level                | <6,5%          | vs | ≥6,5%     |         | <6,5%         | vs | ≥6,5%      |         |
|----------------------------|----------------|----|-----------|---------|---------------|----|------------|---------|
| MACE                       | after 4 months |    |           | p value | after 4 years |    |            | p value |
| In Total                   | 8 (11.3%)      | vs | 4 (19.0%) | 0.690   | 23 (32.4%)    | vs | 11 (52.4%) | 0.387   |
| Death                      | 1 (1.4%)       | vs | 1 (4.8%)  |         | 3 (4.2%)      | vs | 3 (14.3%)  |         |
| Cardiac death              | 1 (1.4%)       | vs | 0         |         | 1 (1.4%)      | vs | 2 (9.5%)   |         |
| Myocardial infarction      | 1 (1.4%)       | vs | 1 (4.8%)  |         | 7 (9.9%)      | vs | 4 (19.0%)  |         |
| PCI/CABG                   | 3 (4.2%)       | vs | 2 (9.5%)  |         | 9 (12.7%)     | vs | 4 (19.0%)  |         |
| Hospitalisation due to CHF | 1 (1.4%)       | vs | 2 (9.5%)  |         | 3 (4.2%)      | vs | 0          |         |
| Stroke                     |                |    | 0         |         | 1 (1.4%)      | vs | 0          |         |
| Diabetes Mellitus          |                |    |           |         | 7 (9,9%)      | vs | 13 (61,9%) | <0,001  |

Among patients with glucose level  $\geq 7,8$  mmol/L concentration of CK and CK-MB was significantly higher during first 48 hours of hospitalization (CK  $p=0,034$ , CKMB  $p=0,01$ ). There was no significant difference between groups regarding TIMI scale, both before ( $p=0,638$ ) and after PCI ( $p=0,372$ ) and Rentrop scale ( $p=0,673$ ).

Among 92 patients, 41 (44,6%) patients had normal glucose metabolism (NGM), 10 (10,9%) were diagnosed with impaired fasting glucose (IFG), 22 (23,9%) impaired glucose tolerance (IGT) and 19 (20,6%) with undiagnosed before diabetes (DM). Analysis of carbohydrate metabolism depending on glucose level on admission is presented in table 2.

In patients with higher levels of glycaemia on admission significantly longer length of hospitalization was observed. Additionally, groups of patients with lower and higher level of glycaemia on admission differed significantly regarding length of hospitalization ( $p=0,028$ ) (Fig. 2).

However, there was no significant difference between investigated groups regarding incidence of MACE in 4 months follow up observation. In 4 year follow up observation group of patients with higher glycaemia on admission had higher incidence of MACE ( $p=0,01$ ) and higher amount of diagnosed cases of diabetes mellitus ( $p=0,011$ ) (Table 3).

Patients characterized by concentration of HbA1c  $\geq 6,5\%$  were older ( $p=0,004$ ), had higher BMI  $>30$  kg/m<sup>2</sup> ( $p=0,019$ ) and lower ejection fraction of left ventricle ( $p=0,003$ ) comparing to those with HbA1c concentration lower than 6,5%. Duration of resting chest pain did not differ significantly in both groups:  $195 \pm 142,67$  [minutes] in group of patients with lower HbA1c concentration and  $210,05 \pm 170,65$  [minutes] in group of patients with higher level of HbA1c ( $p=0,820$ ). Among group of patients with higher concentration of HbA1c mean hospitalization time did not differ significantly comparing to those with lower HbA1c concentration ( $6,17 \pm 4,99$  vs  $5,10 \pm 2,57$  days;  $p=0,857$ ).

Among study population there were no significant differences regarding cardiac markers concentration; CK and CK-MB, angiographic evaluation; TIMI pre and post PCI, TMPG, Rentrop scale. Length of pPCI procedure was significantly higher among patients with glycosylated haemoglobin concentration below 6,5% ( $61,33 \pm 26,95$  [min]) comparing to those with glycosylated haemoglobin concentration above 6,5% ( $45,35 \pm 22,48$  [min]) ( $p=0,032$ ). In group of patients with lower HbA1c more than half of patients ( $n=36$ ; 50,7%) had normal glucose metabolism. Prediabetic state was recognized among 25 patients (35,2%) and diabetes in 10 patients (14,1%) (table 2). Frequency of MACE in 4

month and 4 year observation was comparable. In 4 year follow up higher percentage of diabetes mellitus in patients with HbA1c  $\geq 6,5\%$  was observed (table 4).

## DISCUSSION

Elevated, abnormal glycaemia on admission amongst patients diagnosed with acute myocardial infarction is a common finding. Available literature reports that it occurs among 20% to 50% of patients hospitalized due to acute myocardial infarction, a wide range of percentage values results from different criteria of glucose level.<sup>1,11-13</sup> Values of glycaemia in available literature oscillate from 7,8 mmol/L to more than 11,1 mmol/L and optimal cut off point is hard to determine.<sup>14-17</sup> Increase of glucose level may be a result of many simultaneously ongoing processes related to changes of hormone concentration, organism reaction to stress and insulin resistance. Additionally, intravenous intake of some medications can modify concentration of glucose level during treatment of acute phase of myocardial infarction.

In own study it has been shown, that length of hospitalization due to STEMI was significantly longer in group of patients with higher glycaemia ( $\geq 7,8$  mmol/L) od admission. Cause of prolonged hospitalization was more extensive myocardial injury raised by higher concentration of cardiac markers (CK, CK-MB). Obtained results are consistent with other authors findings.<sup>18,19</sup> Some studies report higher concentration of B-type natriuretic peptide among patients with hyperglycaemia on admission.<sup>20,22</sup> Both parameters are widely recognized as independent factors increasing cardio-vascular risk. On the other hand, present study revealed no significant correlation between initial concentration of cardiac markers and length of prehospital chest pain. That means that investigated patients were treated in optimal time window. In study population, homogenous regarding initial ischemia of cardiomyocytes, impact of other factors, including reactive hyperglycaemia, on further treatment may be less distinctive. It has not been observed that prolonging of prehospital period (measured from the onset of resting chest pain to the admission to cath lab) significantly increased glycaemia on admission. Patients with glycaemia on admission  $\geq 7,8$  mmol/L were characterized with higher incidence of major adverse cardiovascular effects (MACE), but only in 4-year follow-up observation.

In literature impact of reactive hyperglycaemia on prognosis was assessed only in case of exacerbation of different chronic diseases.<sup>1,23</sup> However, unambiguous conclusions affect mostly patients hospitalized due to acute coronary syndromes or ischemic strokes.<sup>24,25</sup> There are many studies, which points out

that among patients with acute myocardial infarction treated with mechanic revascularization or thrombolysis, hyperglycaemia on admission was significant risk factor for increased mortality also intrahospital.<sup>26,27</sup> Some studies revealed that higher glycaemia on admission in that group of patients is linked with worse prognosis.<sup>28-31</sup> Capes et. al in meta-analysis underlines this relationship and additionally noticed that glycaemia between 8,0-10,0 mmol/L associates with 3,9 times higher risk of intrahospital death and glycaemia higher than 10,0 mmol/L on admission was additionally linked with increased risk of heart failure and cardiogenic shock during hospitalisation.<sup>28</sup> In own study, inferior cardio-vascular prognosis was observed only in long-term follow-up. Lack of similar results in intrahospital observation may result from small number of patients or, what is also probable, from inclusion criteria. It would be desirable to perform analysis on higher number of patients with stable and mild course of acute phase of myocardial infarction. Especially since even in that group of patient's significant changes in cardiac marker enzymes and inflammatory parameters (leucocytosis in patients with higher glycaemia on admission) can be found.

Many studies proved, that most patients with coronary artery disease has disturbances in carbohydrate metabolism.<sup>10,32-34</sup> Additionally coexistence of disturbances of carbohydrate metabolism and acute phase of myocardial infarction is frequently observed. Persisting hyperglycaemia through its adverse effect inhibits chemotaxis and phagocytosis of neutrophils (immunological suppression), as well as increases oxygen consumption and potentially exacerbates ischemia. In such conditions, through activation of plasminogen activator inhibitor 1 (PAI-1), increase of coagulation factor VII, XII and fibrinogen, and most of all through increased platelet reactivity prothrombotic features of blood are escalated. Hyperglycaemia additionally reduces amount of nitric oxide and prostacyclin produced by endothelium, attenuating its vasodilative function. This mechanism is particularly important, when hyperglycaemia persists for a longer period of time, because it may lead to disturbances of function of blood vessels resulting from the reactive oxygen species (ROS), even if proper glycaemia was restored.<sup>36,37</sup> This phenomenon, defined as "metabolic memory" and described by S del Prato et al.<sup>38</sup> as Bad glycaemic legacy explains why restrictive control of glycaemia with optimal multifactorial treatment among patients with diabetes not always inhibits progression of micro and macro-vascular complications.

A completely separate issue are cases in which reactive hyperglycaemia may be an undiagnosed previously diabetes.<sup>32,35,36,39</sup> Husband et al. described this relationship in the 1980s. He investigated group of patients with acute myocardial infarction without history of diabetes, but with hyperglycaemia at admission defined as glycaemia >10,0 mmol/L. He noticed, that 1/3 of patients were diagnosed with diabetes after two months since hospital discharge.<sup>39</sup> Also in own study diabetes diagnosed on the basis of oral glucose tolerance test was definitely rarer among patients with glycaemia on admission <7,8 mmol/L than among patients with reactive hyperglycaemia ≥7,8 mmol/L. At the same time, patients with higher blood glucose values on admission who had a negative result of an oral glucose test performed during hospitalization were more likely to develop diabetes in 4-year follow-up. However, frequency of prediabetes in both groups of patients (with lower and higher glycaemia on

admission) was comparable. It should be mentioned, that according to current guidelines both prediabetic states (impaired fasting glucose and impaired glucose tolerance) have different predictive value. Increased mortality was observed only in patients with impaired glucose tolerance, despite the lack of direct relationship with the risk of macroangiopathy.<sup>1</sup> Although reactive hyperglycaemia is transient in many patients and is an expression of broadly defined stress response, it often reflects the latent spectrum of metabolic disorders. Revealing of these disturbances during hospitalization of patients with STEMI before discharge may be the right moment to perform complete diagnostics.

Concentration of glycated haemoglobin indicates glycaemic control in past 3 months, regardless temporary glucose fluctuations. Elevated values reflect chronic hyperglycaemia, which leads to protein glycation and may be helpful in diagnosis of diabetes in patients treated with acute myocardial infarction.<sup>40</sup> In own study around 23% of patients with STEMI had elevated values of HbA1c ≥6,5% and during hospitalization diabetes was diagnosed more often on the basis of oral glucose tolerance test in this group of patients. Even higher percentage of diabetes was observed in group of patients with normal value of OGTT performed during hospitalization in 4 year follow up. However, it should be remembered, that in acute phase of myocardial infarction, disturbances of glucose metabolism may be reversible. Bronisz et al. proves this issue and noticed significantly lower frequency of glucose metabolism disturbances after three months upon discharge, comparing to those gathered during hospitalization. However, this are isolated cases. Most studies underline reliability, security and univocity of mentioned tests in myocardial infarction and become constant part of current guidelines.<sup>1</sup> Thereby, HbA1c seems to be a useful marker of occurrence of distant dysfunction in carbohydrate metabolism and also as useful screening tool constitutes a valuable part of optimal diagnostics.<sup>42</sup> Elevated level in plasma (≥6,5%) may indicate priorly undiagnosed diabetes or state predisposing to glucose metabolism disturbances in future.

Even though in own study, remaining patients were observed with concentration of glycated haemoglobin HbA1c <6,5% and it should be underlined that proper result of HbA1c may occur among patients with significant deterioration of glucose metabolism, whose detectable level of haemoglobin glycation was still not achieved.<sup>43-45</sup>

Mean hospitalization duration and frequency of MACE in 4 month and 4-year follow-up observation were comparable taking into account HbA1c. This observation is contrary to results presented in cited above studies, but also results of investigated group characteristics. Patients with concentration of HbA1c ≥6,5% were more burdened with cardio-vascular risk; were older, more obese, had lower ejection fraction of left ventricle comparing to those with HbA1c <6,5%.

It is possible that impact on final results could have other comorbidities not included in this analysis and different impact of reactive hyperglycaemia as adaptive metabolic response to stress among patients with chronic, untreated hyperglycaemia. Additional modelling factor could be duration of coronary angioplasty procedure of target vessel. Indirectly, it may indicate more advanced atherosclerosis, more intravascular calcifications or more volume of periprocedural contrast usage and thus increased risk of nephropathy.

In conclusion, group of patients with disturbed carbohydrate metabolism had inferior clinical course. In intrahospital observation hospitalization length was longer and in long-term observation occurred more adverse cardio-vascular effects. Probability of development of diabetes in long-term follow – up was higher in group of patients with higher levels of glycaemia on admission and higher concentration of glycated haemoglobin during hospitalization in the course of STEMI.

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