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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Higher admission glycaemia independently of diagnosed or unrecognised diabetes mellitus is a risk factor for failed myocardial tissue reperfusion and higher mortality after primary angioplasty

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Abstract

Background and aim: Admission hyperglycaemia worsens reperfusion in ST-segment elevation myocardial infarction (STEMI). ST-segment elevation resolution parallels myocardial tissue reperfusion and predicts the outcome of primary percutaneous coronary intervention (pPCI).

Methods: We investigated whether higher glycaemia on admission impairs tissue-level reperfusion after pPCI for STEMI, assessed with the single-lead Schröder method of ST-segment resolution analysis (maxSTE).

Results: Among 323 patients (60.4 ± 11.5 years, 27.8% female), 13.4% of nondiabetic subjects and 58.2% of those with known diabetic history (17%) were admitted with glycaemia > 11.1 mmol/L. Failed tissue reperfusion, recognised if high-risk maxSTE criteria were fulfilled, was present among 25% of patients. The overall 180-day mortality rate was 6.8% (n = 22). Admission glycaemia ≥ 8.75 mmol/L appeared as the single risk factor for failed tissue reperfusion (ROC area = 0.638, standard error = 0.038, p < 0.001). Even after adjustment for diabetes history, patients with admission glycaemia ≥ 8.75 mmol/L (44.5%) had 2.36-fold higher risk (95% confidence interval [CI] 1.25–4.46, p = 0.008) of failed tissue reperfusion. After exclusion of patients with known diabetes and those with acute blood glucose level > 11.1 mmol/L (28%), admission glycaemia remained an independent predictor of failed tissue reperfusion (odds ratio [OR] 1.32, 95% CI 1.03–1.69, p = 0.028). Admission glycaemia and failed tissue reperfusion (high- vs. low-risk maxSTE category) were the independent predictors of 180-day mortality (OR 1.18, 95% CI 1.05–1.32, p = 0.004 and OR 3.84, 95% CI 1.12–13.21, p = 0.033, respectively).

Conclusions: Higher admission glycaemia in patients treated with pPCI for STEMI predicts failed myocardial tissue reperfusion and 180-day mortality, independently of prior or acute diabetic status.

Key words: admission hyperglycaemia, resolution of ST-segment elevation, myocardial reperfusion, primary angioplasty

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INTRODUCTION

Hyperglycaemia on admission is an independent and potent risk factor of adverse events after ST-segment elevation myocardial infarction (STEMI), even after adjustment for prior diabetes and glycated haemoglobin level [1–3]. At the same time, unsuccessful tissue-level reperfusion is the primary determinant of unfavourable clinical outcomes after STEMI [4]. Interestingly, in patients treated with primary percutaneous coronary intervention (pPCI) neither the epicardial nor myocardial tissue reperfusion appeared to be affected by the diabetes history [5–8]. Elsewhere, a negative effect of prior diabetes on reperfusion success has been shown, but in the setting of randomised trials with a highly selected patient population and with no adjustment for admission glycaemia [9, 10].

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Until now only a few studies have demonstrated the detrimental impact of admission hyperglycaemia on myocardial tissue-level reperfusion, independently of prior diabetes. However, of note is that in the majority of these studies reperfusion status was assessed directly after pPCI procedure and thus adequate but delayed tissue-level reperfusion was omitted. Furthermore, whether higher admission glycaemia, but below the threshold for diabetes, impairs myocardial tissue-level reperfusion remains not fully investigated [11–13].

Interestingly, it has been proven that ST-segment elevation resolution parallels myocardial tissue reperfusion [14]. What is more, simple and noninvasive analysis of the extent of worse ST-segment deviation persisting in a single-lead up to 3 h after the initiation of reperfusion (maxSTE), apart from the proven prediction of infarct size and prognostic value, was shown to correlate with the extent of myocardial tissue reperfusion after pPCI, as evaluated with positron emission tomography [15, 16].

Therefore, the present study examined the impact of admission glycaemia on the reperfusion efficacy of pPCI as assessed by maxSTE, with the subgroup analysis performed exclusively among patients without known diabetes admitted with blood glucose level ≤ 11.1 mmol/L (200 mg%) [17].

METHODS

Patients

The prospective registry of 369 consecutive, unselected patients treated for STEMI with pPCI within the following 10 months was screened for those who met the inclusion criteria: (1) ST elevation of ≥ 0.1 mV in > 1 limb lead or ≥ 0.2 mV in chest leads; (2) time-to-treatment ≤ 12 h; (3) good quality, diagnostic 12-lead electrocardiogram (ECG) recorded within the 3 h after the pPCI available; and (4) plasma glycaemia measured from a blood sample taken at the time of introducer sheath insertion (just before the pPCI procedure). Patients with left bundle branch blocks and/or ventricular paced rhythm were excluded from the study. The final study population comprised 323 patients. Primary PCI was performed according to the standard techniques, after the loading doses of aspirin and clopidogrel, followed by a typical daily dosing. Glycoprotein IIb/IIIa inhibitor was administered at the discretion of the operator; however, it was encouraged in the case of anterior STEMI or diabetes history. The Local Bioethics Committee approved the study protocol.

ECG analysis

Two independent, experienced observers, blinded to the clinical and procedural data, made qualitative and quantitative analyses of ECGs. ST-deviation was measured using handheld callipers 20 ms after the end of QRS with an accuracy of 0.05 mV. In STEMI of anterior wall ST-elevations from I, aVL, and V1–V6 leads were analysed. In inferior wall STEMI the ST-elevations from either II, III, aVF, V5–V6, or ST-depressions (≥ 0.1 mV) from concomitant V1–V4 leads were assessed, whichever was greater.

MaxSTE risk categories

Consistently, with the well-validated methodology of ST-resolution analysis proposed by Schröder et al. [14] (maxSTE), patients were stratified into the low-, medium-, and high-risk groups upon analysis of the extent of postprocedural ST deviation. Briefly, patients with STEMI of the anterior wall with maximum ST-elevation > 4.5 mm in a single lead of the diagnostic ECG were categorised as being in the high-risk group if the maximum single-lead ST-elevation persisting after the pPCI was > 3 mm, and as low-risk if it was ≤ 2 mm. In the case of anterior STEMI, but with maximal ST-elevation ≤ 4.5 mm, the high-risk group included patients with maximum residual ST-elevation > 5 mm, in contrast to grouping those with the worst persisting ST-elevation ≤ 1 mm to the low-risk category. Patients with STEMI of inferior location were categorised as high-risk if their maximal ST-deviation existing in postprocedural ECG was > 2 mm, in contrary to those in the low-risk group with ≤ 1 mm. Patients with ST-resolution, who did not meet the criteria given above, were stratified as medium-risk by maxSTE.

Unsuccessful myocardial tissue reperfusion was considered to have occurred in patients stratified as high-risk by maxSTE.

Known diabetes history was defined as a previous diagnosis of diabetes treated with diet, oral medication, or insulin.

A clinical history of risk factors such as arterial hypertension, hypercholesterolaemia, and smoking was determined from a patient history taken or medical records.

Coronary angiography

The analysis was performed off-line. The number of diseased vessels and pre- and postprocedural Thrombolysis in Myocardial Infarction (TIMI) flow grade was assessed by two observers blinded to the clinical and laboratory results. If differences in individual assessment occurred, an agreement between observers was reached by consensus.

Follow-up

The 180-day mortality was evaluated based on medical records, prospective data obtained from an outpatient clinic, written correspondence and telephone calls, as well as PESEL register data.

Statistical analysis

Continuous data are presented as the mean ± standard deviation and were compared by use of Kruskal-Wallis one-way or Mann-Whitney U tests. Categorical data are presented as frequencies and were compared by Pearson χ^2 or Fisher's exact tests. The Spearman's correlation coefficient was used for bivariate correlations. Analysis of receiver operating characteristics curve (ROC) was used for evaluation of admission

blood glucose level performance in discrimination of the high-risk maxSTE category and to define the optimal cut-off point. The 180-day all-cause mortality was presented on the graphs as Kaplan-Meier curves with p-value of the Log Rank test. Binary logistic regression with applied backward Wald stepwise method was used for identification of independent risk factors of the high-risk maxSTE and 180-day mortality. Since maxSTE stratifies patients essentially into those of excellent (low-risk) versus those of poor outcome (high-risk group), we searched for determinants of the high-risk with the low-risk maxSTE category as the reference. Multivariate analyses were adjusted for age, female gender, prior diabetes, smoking habit, hypertension history, prior myocardial infarction, anterior STEMI, pre- and postprocedural TIMI grade 3 flow, time-to-treatment, multivessel disease (more than one of diseased vessels), and the following evaluated on admission: blood glucose level (mmol/L), heart rate (bpm), systolic blood pressure (mmHg), and Killip class > 1. Separate analyses of the high-risk maxSTE risk factors were done for: (1) the overall studied group; and (2) exclusively among the patients without known diabetes history and admitted with glycaemia ≤ 11.1 mmol/L [17]. Significance was assumed at the two-tailed p-value of ≤ 0.05.

RESULTS

Patient characteristics

Among the 323 patients (mean age 60.4 ± 11.5 years, 27.8% female) who met the study inclusion criteria, 17% were patients with known diabetes, 21.1% had admission glycaemia > 11.1 mmol/L (diabetic threshold), and 28.2% were either previously diagnosed diabetic subjects or had acute glycaemia > 11.1 mmol/L. There were 13.4% nondiabetic patients and 58.2% of patients with known diabetic history, who had admission glycaemia above the diabetic threshold. Mean time to treatment was 4.8 ± 2.4 h. The overall 180-day mortality rate was 6.8% (n = 22). Detailed patient characteristics are shown in Table 1.

A significant but low correlation was found between blood glucose levels and heart rate assessed on admission (r = 0.156, p = 0.007). Admission glycaemia correlated also with the extent of maximal ST-segment deviation identified in a single-lead of diagnostic ECG and with peak creatine phosphate kinase muscle-brain levels (r = 0.194, p < 0.001 and r = 0.189, p = 0.013; respectively).

MaxSTE risk categories and admission glycaemia

Based on maxSTE, 43% of patients were classified in the low-risk, 31.9% in the medium-risk, and 25.1% in the high-risk group. Gradual pattern of differences noted in clinical and procedural data among patients from various maxSTE groups is shown in Table 2. Whereas higher admission blood glucose levels were ascertained for the higher maxSTE risk categories, there were no differences in the prevalence of known diabetes. However, gradually more patients from the groups of rising maxSTE risk category presented with glycaemia ≥ 11.1 mmol/L (Table 2).

In the subgroup of patients including individuals with known diabetes and those with admission blood glucose level > 11.1 mmol/L (28%), 31.9% were stratified as high risk, constituting 35.8% of all high-risk maxSTE subjects.

The ROC proved that admission hyperglycaemia is the single risk factor of high-risk maxSTE (area = 0.638, standard error = 0.038, p < 0.001), and its optimal cut-off point was set at 8.75 mmol/L (158 mg%) (0.625 sensitivity and 0.595 specificity). The comparison of clinical and procedural data between the groups of patients dichotomised/distinguished upon the established glycaemic cut-off point is presented in Table 1. Subjects admitted with blood glucose level ≥ 8.75 mmol/L were categorised more often as high risk by maxSTE than those with lower glucose levels (35.0% vs. 18.3%, respectively, p = 0.004). The Kaplan-Meier survival curves plotted for a 180-day follow-up for patients with admission glycaemia of ≥ vs. < 8.75 mmol/L and for patients in the low-, medium-, and high-risk maxSTE groups are shown in Figure 1. Among patients admitted with acute glycaemia ≥ 8.75 mmol/L significantly more subjects died by 180 days as compared to those presenting with lower blood glucose levels (n = 15/44; 10.4% vs. n = 7/17; 93.9%; p = 0.026, respectively). The 180-day mortality rate in the low- and medium-risk maxSTE groups was low and similar (n = 4/139; 2.9% vs. n = 4/103; 3.9%; p = NS, respectively). However, significantly more patients in the high-risk maxSTE group died during the six-month follow-up (n = 14/81; 17.3%, p < 0.001).

Predictors of high-risk maxSTE and 180-day mortality

Table 3 shows the univariate and multivariate predictors of high-risk maxSTE. Although known diabetes did not predict high-risk maxSTE, admission glycaemia remained an independent risk factor of the high-risk maxSTE, both (1) in the whole studied population; and (2) in the subgroup of patients limited to those without known diabetes and admitted with blood glucose level ≤ 11.1 mmol/L. Overall, patients admitted with glycaemia ≥ 8.75 mmol/L had a 2.36-fold higher risk of being stratified as high-risk by maxSTE, independently of diabetes history (p = 0.008).

Importantly, admission glycaemia and maxSTE (high- vs. low-risk category) were both independent risk factors of the 180-day mortality (odds ratio [OR] 1.18, 95% confidence interval [CI] 1.05–1.32, p = 0.004 and OR 3.84, 95% CI 1.12–13.21, p = 0.033, respectively), along with unsuccessful TIMI 3 restoration (OR 3.6, 95% CI 1.2–10.6, p = 0.018), patient's age (p = 0.170), and Killip class > 1 assessed on admission (p = 0.091).

DISCUSSION

Our results indicate that higher admission glycaemia, but not diabetes history, is a risk factor for failed myocardial

Table 1. Differences in clinical, angiographic, electrocardiographic, and procedural data between groups of patients dichotomised by the established glycaemic cut-off point of 8.75 mmol/L

	All patients (100%, n = 323)	Patients admitted with blood glucose level ≥ 8.75 mmol/L (44.6%, n = 144)	Patients with admission blood glucose level < 8.75 mmol/L (55.4%, n = 179)	p*
Demographics, risk factors, and clinical history				
Age [years]	60.4 ± 11.5	62.0 ± 11.2	58.9 ± 11.6	0.016
Female	27.8%	34.3%	20.7%	0.008
Anterior STEMI	44.3%	45.5%	42.1%	0.315
Known diabetes history	17.0%	31.3%	5.0%	< 0.001
Known diabetes history or admission glycaemia > 11.1 mmol/L	28.2%	56.6%	4.9%	< 0.001
Current and prior smokers	76.5%	81.7%	70.65%	0.022
Hypercholesterolaemia	75.6%	76.3%	76.5%	0.970
Hypertension	47.95	49.7%	47.0%	0.637
Prior myocardial infarction	17.0%	14.7%	18.9%	0.326
Time-to-treatment [h]	4.8 ± 2.4	4.5 ± 2.3	4.9 ± 2.4	0.175
Admission clinical data and results of biomarkers measurements				
Admission blood glucose level [mmol/L]	9.4 ± 3.5	12.0 ± 3.6	7.1 ± 1.0	< 0.001
Systolic blood pressure on admission [mmHg]	136.8 ± 28.5	134.2 ± 29.1	139.8 ± 27.6	0.054
Heart rate on admission	78.8 ± 17.3	81.4 ± 19.3	76.7 ± 15.5	0.015
Killip class > 1 at admission	11.5%	13.3%	9.8%	0.332
Cardiogenic shock at admission	3.7%	5.6%	1.2%	0.032
Peak CK [U/L]	2019.4 ± 2193.5	2103.6 ± 2696.9	1904.5 ± 1722.4	0.482
Peak CK-MB [U/L]	135.6 ± 280.0	171.2 ± 367.8	101.5 ± 128.9	0.025
Electrocardiogram				
Pre-maximal ST-deviation [mm]	4.5 ± 3.2	5.0 ± 3.5	4.1 ± 2.9	0.007
Post-maximal ST-deviation [mm]	2.1 ± 1.7	2.4 ± 1.8	1.9 ± 1.7	0.006
Angiographic and procedural data				
Multivessel disease	48.1%	50.4%	47.2%	0.588
Culprit lesion stented	81.1%	83.4%	80.4%	0.705
Abciximab administration	50.3%	51.4%	48.8%	0.647
Pre-TIMI grade 3 flow	14.2%	12.8%	14.6%	0.637
Post-TIMI grade 3 flow	81.7%	78.3%	85.4%	0.108

Data are shown as mean ± standard deviation or percentage. *p value for comparison between groups dichotomised by the established glycaemic cut-off point of 8.75 mmol/L. CK — serum creatine kinase; CK-MB — creatine phosphate kinase muscle-brain; Post — postprocedural; Pre — preprocedural; STEMI — ST-segment elevation acute myocardial infarction; TIMI — Thrombolysis in Myocardial Infarction

tissue-reperfusion after pPCI in STEMI, and this consequently results in a larger infarct size and is related to a higher 180-day mortality. Interestingly, higher admission glycaemia remained an independent determinant of unsuccessful tissue-reperfusion even among the patients who had no diabetes history and were admitted with acute glycaemia level below the diabetic threshold (random-admission blood glucose level ≤ 11.1 mmol/L). Namely, an increase of 1 mmol/L (18 mg%) in admission blood glucose level was associated with 12% and 33% increase in the risk of failed reperfusion in the overall studied group and in patients without diabetes or acute glycaemia > 11.1 mmol/L, respectively. Admission glycaemia appeared also the single risk factor of failed myocardial tissue-reperfusion with the resultant 2.36-fold higher risk of failed myocardial tissue-reperfusion and larger infarct size in patients admitted with acute glycaemia ≥ 8.75 mmol/L (≥ 158 mg%). As a result, an increase of 1 mmol/L in admission blood glucose level was associated with an 18% increase in the 180-day mortality risk.

Table 2. Observed differences in clinical, angiographic, and electrocardiographic data among the maxSTE categories

	Low-risk (43.0%, n = 139)	Medium-risk (31.9%, n = 103)	High-risk (25.1%, n = 81)	p*	p†
Demographics, risk factors, and clinical history					
Age [years]	59.2 ± 10.9	60.4 ± 12.3	62.2 ± 11.5	0.113	0.040
Female	24.5%	31.1%	28.4%	0.514	0.406
Anterior STEMI	33.1%	57.3%	46.9%	< 0.001	0.007
Known diabetes history	14.4%	19.4%	18.5%	0.541	0.347
Admission glycaemia > 11.1 mmol/L	15.1%	21.4%	30.9%	0.022	0.007
Known diabetes history or admission glycaemia > 11.1 mmol/L	21.6%	31.1%	35.8%	0.057	0.010
Current plus prior smokers	81.3%	68.0%	74.1%	0.057	0.102
Hypercholesterolaemia	73.9%	76.6%	77.2%	0.828	0.553
Hypertension	48.9%	45.6%	49.4%	0.843	0.946
Prior myocardial infarction	14.4%	18.4%	19.8%	0.533	0.273
Time-to-treatment [h]	4.7 ± 2.3	5.0 ± 2.5	4.6 ± 2.4	0.350	0.782
Admission clinical data and results of biomarker measurements					
Admission blood glucose [mmol/L]	8.9 ± 3.2	9.3 ± 4.0	10.2 ± 3.3	0.003	0.002
Admission glycaemia ≥ 8.75 mmol/L	40.9%	41.1%	62.5%	0.004	0.004
Systolic blood pressure on admission [mmHg]	133.7 ± 24.2	143.1 ± 33.0	133.9 ± 28.3	0.041	0.475
Heart rate on admission [bpm]	77.4 ± 18.1	80.3 ± 15.9	79.3 ± 17.8	0.241	0.178
Killip class > 1 at admission	6.5%	12.6%	18.5%	0.023	0.006
Cardiogenic shock at admission	1.4%	4.9%	6.2%	0.153	0.056
Peak CK [U/L]	1832.3 ± 2266.3	2060.4 ± 1749.9	2324.1 ± 2591.7	0.047	0.026
Peak CK-MB [U/L]	91.0 ± 136.7	135.9 ± 152.1	200.6 ± 476.4	0.011	0.003
Electrocardiogram					
Pre-maximal ST-elevation [mm]	3.4 ± 2.2	4.3 ± 2.8	6.7 ± 4.1	< 0.001	< 0.001
Post-maximal ST-deviation [mm]	0.8 ± 0.6	2.2 ± 0.7	4.3 ± 1.7	< 0.001	< 0.001
Angiographic and procedural data					
Multivessel disease	51.4%	34.3%	60.0%	0.002	0.685
Culprit lesion stented	79.9%	79.4%	85.2%	0.546	0.408
Abciximab administration	39.1%	54.4%	64.2%	< 0.001	< 0.001
Pre-TIMI grade 3 flow	21.6%	10.7%	6.3%	0.004	0.001
Post-TIMI grade 3 flow	90.6%	76.7%	72.8%	0.001	< 0.001

Data are shown as mean ± standard deviation or percentage. *Pearson χ^2 or Fisher's exact tests for categorical data and Kruskal-Wallis test for comparison of continuous data. †Spearman correlation for a trend across the three groups. CK — serum creatine kinase; CK-MB — creatine phosphate kinase muscle-brain; Post — postprocedural; Pre — preprocedural; STEMI — ST-segment elevation acute myocardial infarction; TIMI — Thrombolysis in Myocardial Infarction

The current results are in line with higher incidence of no-reflow phenomenon and resultant larger infarctions and worse functional recovery in patients admitted with acute glycaemia ≥ 160 mg% and treated with pPCI, regardless of the preceding diabetic status, as reported by Iwakura et al. [11].

However, it has not been established whether higher admission glycaemia has a direct influence or is instead a marker of the pathophysiologic process related to unsuccessful myocardial reperfusion.

The overall 17% prevalence of known diabetes history among the unselected patients with STEMI examined in the present study is similar to previously reported results [5–7, 9, 10]. Furthermore, the 13.4% rate of no evidence of known diabetes admitted with random-admission blood glucose level > 11.1 mmol/L documented currently is also in accordance with others' findings [18]. Interestingly, acute glycaemia level in patients without known diabetes admitted with STEMI was not influenced by the preceding chronic glycometabolic

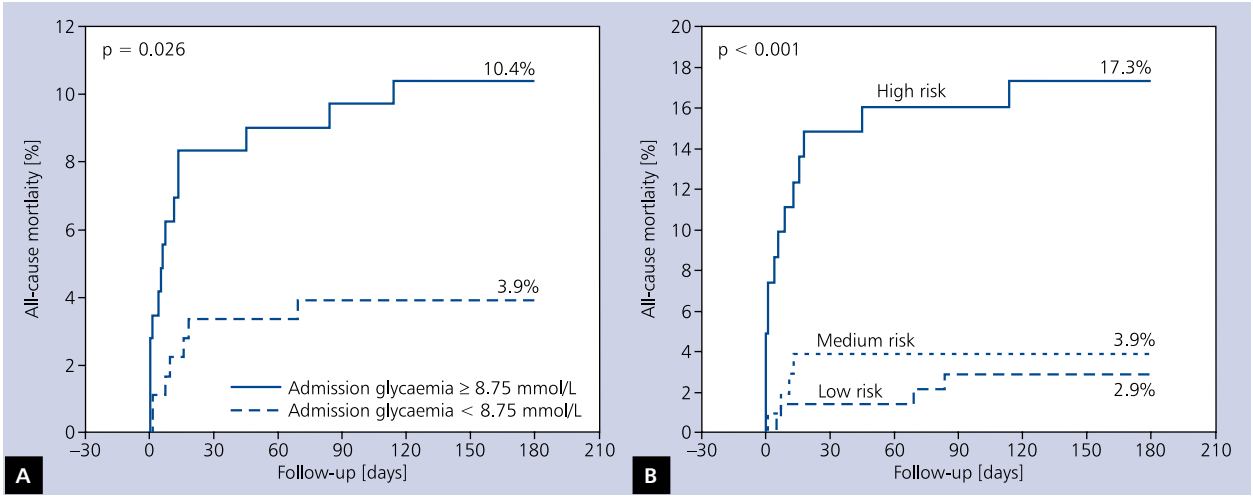

Figure 1. The Kaplan-Meier survival curves plotted for a 180-day follow-up, individually for patients admitted with acute glycaemia ≥ vs. < 8.75 mmol/L (**A**) and for patients in the low-, medium-, and high-risk maxSTE groups (**B**)

Table 3. Univariate and multivariate predictors of the high-risk maxSTE category (OR and 95% CI for comparison between the high- vs. the low-risk category)

	Univariate predictors of the high-risk maxSTE			Multivariate predictors of the high-risk maxSTE		
	OR	95% CI	p	OR	95% CI	p
All patients						
Admission blood glucose [mmol/L]	1.12	1.03–1.22	0.010	1.12	1.01–1.24	0.027
Admission glycaemia ≥ 8.75 mmol/L*	2.41	1.36–4.26	0.002	2.36	1.25–4.46	0.008
Anterior STEMI	1.79	1.02–3.13	0.043	–	–	–
Killip class > 1 on admission	3.28	1.36–7.90	0.008	–	–	–
Known diabetes history	1.35	0.65–2.82	0.420	–	–	–
Preprocedural TIMI flow grade < 3	4.07	1.51–10.97	0.006	2.54	0.89–7.25	0.082
Postprocedural TIMI flow grade < 3	4.01	1.93–8.35	< 0.001	3.03	1.32–6.93	0.009
Patients without known diabetes history and admitted with acute glycaemia ≤ 11.1 mmol/L						
Admission blood glucose [mmol/L]	1.33	1.07–1.66	0.012	1.32	1.03–1.71	0.030
Anterior STEMI	2.33	1.19–4.57	0.014	–	–	–
Killip class > 1 on admission	8.03	2.45–26.34	< 0.001	9.77	2.40–39.86	0.002
Multivessel disease	2.25	1.13–4.49	0.021	–	–	–
Preprocedural TIMI flow grade < 3	2.90	0.95–8.92	0.063	–	–	–
Postprocedural TIMI flow grade < 3	5.15	2.15–12.35	< 0.001	4.94	1.80–13.56	0.002

*8.75 mmol/L — the optimal glycaemic cut-off point predictive of the high-risk maxSTE category (c-statistic = 0.638, p < 0.001), entered into the multivariate model as the categorical replacement for the continuous variable of admission blood glucose; CI — confidence interval; OR — odds ratio; STEMI — ST-segment elevation acute myocardial infarction; TIMI — Thrombolysis in Myocardial Infarction

state [19]. On the other hand, the highest (> 10 mmol/L) acute glucose concentrations are encountered more often in patients with either known or with pre-existing but undiagnosed diabetes [20].

Nevertheless, the current results showing detrimental and independent influence of higher admission glycaemia on the myocardial tissue-reperfusion even in the absence of diabetes mellitus (either acute or by history) seem to indicate that acute rather than chronic (e.g. pre-existing microvascular status) mechanisms account for this effect.

The results of myocardial blush analysis from the CADILLAC trial showed strong association between depressed baseline left ventricle function and unsuccessful (final blush grade < 3) reperfusion after pPCI. Interestingly, diabetes his-

tory was not associated with failed myocardial tissue reperfusion [8]. Other studies also pointed to acute heart failure as one of the strongest risk factors of failed myocardial reperfusion after pPCI [21]. Interestingly, in the current study there was significant but low positive correlation between acute glycaemia and signs of acute heart failure; admission heart rate, along with the absence of relation between measured on admission blood glucose levels and systolic blood pressure. Moreover, acute heart failure defined as admission Killip class > 1 was present similarly often in patients with acute glycaemia below and above the value predictive of failed reperfusion. Consequently, our results support the notion that higher admission glycaemia, while probably related to the autonomic drive, is not just a simple reflection of the acute haemodynamic condition.

In summary, current results indicate that higher acute glycaemia is not merely an epiphenomenon of 'disease severity' but appeared to be causally associated with reperfusion efficacy of pPCI and consequent unfavourable clinical outcome. The presented results seem to provide a pathophysiological explanation for previous studies that demonstrated the negative impact of admission hyperglycaemia on the clinical outcome after thrombolysis or pPCI in STEMI, observed in patients with and without known diabetes [1, 22].

There are several potential pathophysiological mechanisms underlying the causal and harmful role of acutely elevated glycaemia in failed myocardial tissue reperfusion after pPCI [22]. Acute hyperglycaemia per se is associated with reduced plasma fibrinolytic capacity as reflected by an increased plasminogen activator inhibitor-1 and a decreased tissue plasminogen activator plasma activity. Platelet aggregability, assessed by means of the number of small platelet aggregates measured with a laser-light scattering method, increases in parallel with glucose level [23, 24].

The present results correspond well with outcomes of the DIGAMI trial, which proved that intensive insulin treatment of either individuals with known diabetes or subjects with newly detected diabetes (admission glycaemia > 11.1 mmol/L) during an acute phase of STEMI attenuate a harmful effect of high admission glycaemia with less treatment effect observed during the long-term follow-up [17, 25]. Furthermore, the current results seem to extend findings of DIGAMI, supporting the strategy of early and intensive insulin therapy for patients treated with pPCI and presenting with acutely elevated blood glucose concentration. More importantly, our findings should encourage clinical efforts targeted at a "tight" acute glycaemic control in all diabetic patients after acute myocardial infarction, regardless of the diabetes history and even in those with admission glycaemia below the diabetic threshold.

Limitations of the study

The present study was a retrospective analysis of the prospectively collected data. Routine measurements of the HbA1c concentration and regular performance of oral glucose tolerance test were not done. Certainly, a lack of systemic application of other and more direct methods of myocardial tissue-level reperfusion evaluation, e.g. myocardial blush analysis, constitutes a significant limitation of the current study.

Furthermore, data on left ventricular ejection fraction during the acute phase of myocardial infarction, time of last meal, severity of pain, intensity of anxiety, duration of diabetes mellitus, and type of antidiabetic treatment, which unfortunately was incomplete, would undoubtedly improve interpretation of the current results.

CONCLUSIONS

Higher admission blood glucose levels in patients treated with pPCI is associated with more frequent failed myocardial tissue-level reperfusion and in consequence smaller myocardial salvage and worse mid-term clinical outcome. What is more, this effect was a risk factor independent of known diabetes and regardless of the acute diabetic status, which may be due to a 'newly detected' diabetes. Thus, it appeared that admission blood glucose levels, but not diabetes history, should guide additional therapeutic interventions aimed at the restoration of adequate myocardial tissue-level reperfusion after pPCI.

Conflict of interest: *none declared*

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