# The effects of acute hyperglycaemia on the in-hospital and long-term prognosis in patients with an acute coronary syndrome — a pilot study

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#### Abstract

**Background:** Acute hyperglycaemia is an adverse prognostic factor in patients with acute coronary syndrome (ACS). It is unclear whether these negative effects apply equally to patients with diabetes mellitus (DM) and non-DM patients.

**Aim:** To evaluate the short-term (in-hospital) and long-term (four-year) prognostic value of acute hyperglycaemia in ACS patients with or without DM.

**Methods:** The study involved 116 ACS patients admitted between 2004 and 2006 to our department, who were selected for invasive treatment and who had both admission and first fasting glucose levels measured. Patients were classified as DM (n = 23), on the basis of a known history of diabetes or newly detected diabetes, or non-DM (n = 93). Acute hyperglycaemia was defined as an admission glycaemia ≥ 10.0 mmol/L (180 mg/dL) for non-DM patients, or ≥ 7.8 mmol/L (140 mg/dL) for DM patients, or a first fasting glucose level ≥ 5.6 mmol/L (100 mg/dL) for both DM and non-DM patients. The primary end-point was defined as mortality during follow-up. The secondary end-points were death, cardiac arrest or repeated ACS occurrence, stroke or transient ischaemic attack, and the need for repeat percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) procedure during the in-hospital and four-year post-hospital periods. During follow-up, patients were assessed for a composite end-point defined as all-cause death, repeated ACS occurrence, repeat PCI or CABG procedure, and stroke.

**Results:** Acute hyperglycaemia was present in 28 non-DM and 14 DM patients. The mean follow-up time was  $4 \pm 0.6$  years. For DM patients, there was no significant difference in four-year mortality between hyperglycaemic and normoglycaemic patients (14.3% vs 11.1%, respectively; NS). The occurrence of secondary end-points and composite end-point frequency was also similar for these subgroups, both for in-hospital and four-year observations. For non-DM patients, the four-year mortality was similar for hyperglycaemic and normoglycaemic subjects (17.9% vs 10.8%, respectively; NS), whereas cardiac arrest during the in-hospital period was more common for hyperglycaemic than normoglycaemic patients (3.6% vs 0.0%, respectively; n = 1 vs 0; p = 0.01). The composite end-point for the in-hospital period was reached by 17.6% of hyperglycaemic and 13.8% of normoglycaemic non-DM patients (NS). The composite end-point during the four-year observation period was more frequently reached in hyperglycaemic than in normoglycaemic non-DM patients (78.6% vs 56.9%, respectively; p = 0.04).

**Conclusions:** Acute hyperglycaemia in non-DM patients hospitalised due to ACS was found to be an unfavourable long-term (four-year) risk factor, and may also be an unfavourable in-hospital risk factor. In contrast, acute hyperglycaemia did not affect cardiovascular outcomes in DM patients.

Key words: diabetes, hyperglycaemia, acute coronary syndrome, risk factor

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# **INTRODUCTION**

Abnormal glucose metabolism including impaired fasting glycaemia, impaired glucose tolerance and diabetes mellitus (DM) are important and independent ischaemic heart disease risk factors, and have a negative impact on outcomes of patients with an acute coronary syndrome (ACS) [1].

Acute hyperglycaemia is also known as hyperglycaemia of the acute phase, or stress hyperglycaemia, and is defined as an increase in blood glucose level due to acute, severe injury (e.g. ACS). Recent studies have reported that elevated glucose level in ACS patients was associated with an increased risk of in-hospital and long-term complications, both in DM and non-DM patients [2, 3]. Increased glucose levels at admission are associated with a higher Killip class, a larger infarct and worse left ventricular (LV) function [4]. In-hospital infections, pulmonary oedema, ventricular tachycardia, atrial fibrillation, ventricular fibrillation, pre-hospital and in-hospital cardiac arrest or cerebrovascular incidents have also been reported as being more frequent in patients with elevated glucose levels at admission [4].

There are limited data regarding the effects of acute hyperglycaemia on long-term outcomes in ACS patients with or without DM. Only a few studies with follow-up longer than one year investigated the prognostic value of acute hyperglycaemia in DM patients and non-DM subjects. Moreover, these studies used different definitions of hyperglycaemia, which were based on a single glucose measurement, either at admission or at first fasting [3, 5].

The present study investigated the effects of hyperglycaemia in ACS patients with and without DM on the short-term (in-hospital) and long-term (four-year) outcomes.

# **METHODS**

# Study population

The study involved patients who were selected for an urgent invasive diagnosis and treatment of ischaemic heart disease and were hospitalised due to ACS between 2004 and 2006 in our department. The ACS was defined as unstable angina, myocardial infarction with ST segment elevation (STEMI), or MI without ST segment elevation (NSTEMI). The study recruited 116 patients who agreed to participate and whose glycaemic status during hospitalisation was known. Both admission glycaemia and first fasting glycaemia were measured. In patients without previously known diabetes, an oral glucose test (OGTT) was performed on or after the fourth day of hospitalisation to identify any glucose metabolism abnormalities. In case of multiple hospitalisations due to ACS during the study period, only data from the first hospitalisation were analysed. We evaluated demographic data, angiographic parameters, i.e. percutaneous coronary intervention (PCI) procedure, effectiveness of PCI on the basis of the TIMI scale where TIMI 3 flow was considered as effective, three-vessel

coronary artery disease (CAD) presence, electrocardiographic changes and selected biochemical measurements, i.e. maximum levels of troponin I and creatine kinase, lipidogram, glucose levels on admission and at first fasting, and OGTT results. Patients were assessed for the presence of the following risk factors in their history and up to the final follow-up visit: smoking status, obesity (body mass index  $> 30 \text{ kg/m}^2$ ), hypertension (systolic pressure ≥ 140 mm Hg and/or diastolic pressure ≥ 90 mm Hg), and hypercholesterolaemia (total cholesterol level ≥ 4.5 mg/dL or LDL cholesterol level > 2.5 mg/dL). All patients underwent echocardiography (HP Sonos 5500) to assess LV ejection fraction (LVEF) (Teihcholz's or Simpson's method or eyeball evaluation of two-dimensional projections). Four-year follow-up data was obtained during visits (99 patients) or via telephone or written questionnaires (17 patients).

Glucose concentration was measured from venous blood samples on admission and the next day following an overnight fast of more than eight hours (i.e. first fasting). For analysis, patients were placed into DM or non-DM groups. The DM group consisted of patients known to have DM, and patients who were not previously known to have DM but were newly diagnosed with DM during hospitalisation on the basis of OGTT performed at the end of hospitalisation (i.e. after the acute phase of ACS, on or after the fourth day of hospitalisation). A diagnosis of DM was based on a glucose level ≥ 11.1 mmol/L 120 min after a 75-g oral glucose load. The non-DM group consisted of the remaining patients.

All patients were categorised as normoglycaemic or hyperglycaemic based on both admission and first fasting glucose levels. Adhering to the recommendations of the Polish Diabetic Association for hypoglycaemic treatment in states of "relative hypoglycaemia", patients were classified as hyperglycaemic if the admission glucose level was  $\geq$  7.8 mmol/L (140 mg/dL) for DM patients or  $\geq$  10.0 mmol/L (180 mg/dL) for non-DM patients [6], or if the first fasting glucose level was  $\geq$  5.6 mmol/L (100 mg/dL) for either DM or non-DM patients.

# **End-points**

The primary end-point was defined as mortality during the four-year follow-up period. Secondary end-points were defined as death, sudden cardiac arrest, repeated MI, stroke or transient ischaemic attack (TIA), and the need for coronary artery bypass grafting (CABG) or PCI (both elective and unscheduled) during the in-hospital and four-year follow-up periods.

The composite end-point for in-hospital stay was defined as the occurrence of at least one of the following: death, sudden cardiac arrest, repeated MI, stroke or TIA, the need for urgent CABG, and repeated PCI. The composite end-point for the four-year follow-up was defined as the occurrence after hospitalisation at least one of the following: death from any cause, repeated MI, PCI, CABG, stroke or TIA.

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The study protocol was approved by the Bioethics Committee of Jagiellonian University (KBET/47/B/2010).

# Statistical analysis

Continuous variables with normal distribution are presented as mean  $\pm$  SD, and differences were analysed using Student's t-test. The non-parametric Mann-Whitney U test was used to compare non-normally distributed variables. The  $\chi^2$  test was used to determine the significance of associations between categorical variables. If expected frequencies were less than five, a  $\chi^2$  tests with Yates' correction was used, and Fisher's exact test was used when the total number of observations was small. A p value <0.05 was considered significant. Statistical analysis was performed using Statistica PL software version 8.0.

### **RESULTS**

Of the 116 patients, 23 were classified as DM (including five patients with newly diagnosed DM) and 93 were classified as non-DM. The mean follow-up period was  $4\pm0.6$  years (> four years in 62% of patients). In both the DM and the non-DM group, normoglycaemic and hyperglycaemic pa-

tients did not differ with respect to age, sex, incidence of hypertension, hypercholesterolaemia, smoking, obesity, type of ACS or the distribution of arteries responsible for ACS (Tables 1, 2). In DM patients, hyperglycaemia and normoglycaemia groups did not differ in the frequency of history of MI. In-hospital mortality tended to be higher in non-DM than DM patients (13.0% vs 3.2%; p=0.06) whereas mortality after hospitalisation was similar (15.0% vs 15.1%; p=0.95, respectively).

# Subjects with diabetes mellitus

Of the 23 DM patients, 14 (61%) were classified as hypergly-caemic, and nine (39%) were classified as normoglycaemic (Table 1). During the in-hospital period, hyperglycaemic DM patients were more commonly found to have three-vessel CAD than normoglycaemic DM patients (35.7% vs 0.0%; p=0.04). Although hyperglycaemic DM patients tended to undergo PCI less frequently than normoglycaemic DM patients, the difference was not significant (71.4% vs 100.0%; p=0.08). The incidence of TIMI 3 flow after the procedure was similar in both groups (Table 2). In hyperglycaemic DM patients with STEMI, the biomarkers for myocardial necrosis

**Table 1.** Comparison of baseline demographic and clinical characteristics as well as in-hospital parameters between hyperglycaemic and normoglycaemic patients

	Patients with DM (n = 23)			Patients without DM (n = 93)		
	Hyperglycaemia	Normoglycaemia	Р	Hyperglycaemia	Normoglycaemia	P
	N = 14 (61%)	N = 9 (39%)		N = 28 (30%)	0%) N = 65 (70%)	
Age [years] [median;	61.6 ± 9.5	60.4 ± 9.7	0.33	61.4 ± 12.1	61.3 ± 12.1	0.98
interquartile range]	[67; 57–73]	[57; 53–70]		[60; 53–70]	[63; 51–70]	
Male gender	9 (64.3%)	4 (44.4%)	0.61	25 (89.3%)	53 (81.53%)	0.29
Hypertension	13 (92.8%)	8 (88.9%)	0.74	18 (64.3%)	50 (76.9%)	0.21
Hypercholesterolaemia	8 (57.1%)	4 (44.4%)	0.87	16 (57.1%)	39 (60.0%)	0.80
Smokers	4 (28.6%)	2 (22.2%)	0.88	13 (46.4%)	26 (40.0%0	0.56
Obesity	4 (28.6%)	3 (33.3%)	0.82	6 (21.4%)	4 (6.2%)	0.08
History of previous MI	4 (28.6%)	3 (33.3%)	0.82	4 (14.3%)	21 (32.3%)	0.07
Glucose level on admission	$12.34 \pm 4.53$	$6.23 \pm 1.05$	0.01	$8.81 \pm 3.23$	$6.69 \pm 2.95$	0.01
(mean mmol/L) [median; interquartile range]	[10.5; 9–15.7]	[6.7; 5.4–6.8]		[8.0; 6.9–9.7]	[6.35; 5.7–72]	
First fasting glucose level	$9.54 \pm 3.74$	$5.53 \pm 0.31$	0.02	$6.23 \pm 0.93$	$5.22 \pm 0.89$	0.01
(mean mmol/L) [median; interquartile range]	[7.3; 6.5–12.1]	[5.45; 5.4–5.5]		[6.15; 5.6–6.7]	[5.1; 4.66–5.45]	
STEMI	10 (71.4%)	6 (66.7%)	0.80	21 (75.0%)	44 (67.7%)	0.48
NSTEMI	3 (21.4%)	3 (33.3%)	0.88	4 (14.3%)	19 (29.2%)	0.12
Unstable angina	1 (7.1%)	0 (0%)	0.82	3 (10.7%)	2 (3.1%)	0.66
Anterior wall MI	4 (28.6%)	1 (11.1%)	0.63	7 (25.0%)	10 (15.4%)	0.27
Newly detected DM	2 (14.3%)	3 (33.3%)	0.57	_	_	_

DM — diabetes mellitus; MI — myocardial infarction; NSTEMI — non-ST segment elevation myocardial infarction; STEMI — ST segment elevation myocardial infarction

Table 2. Comparison of angiographic characteristics between hyperglycaemic and normoglycaemic patien	Table 2. Compa	arison of angiograp	nic characteristics between	hyperglycaemic and	l normoglycaemic patien
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	Patients with DM (n = 23)			Patients without DM (n = 93)		
	Hyperglycaemia	Normoglycaemia	Р	Hyperglycaemia	Normoglycaemia	P
	N = 14 (61%)	N = 9 (39%)		N = 28 (30%)	N = 65 (70%)	
Baseline TIMI 0–1	11 (78.6%)	5 (55.6%)	0.24	17 (60.7%)	31 (47.7%)	0.25
TIMI 3 after PCI	10 (100%)	9 (100%)	-	21 (100%)	51 (98.1%)	0.52
IRA:						
LMCA	0 (0%)	0 (0%)	-	1 (3.6%)	6 (9.2%)	0.60
LAD	6 (42.9%)	4 (44.4%)	0.72	11 (39.3%)	24 (36.9%)	0.82
Cx	1 (7.1%)	0 (0%)	0.82	3 (10.7%)	10 (15.4%)	0.78
RCA	7 (50.0%)	4 (44.4%)	0.86	6 (21.4%)	13 (20.0%)	0.93
Single-VD	4 (28.6%)	4 (44.4%)	0.74	9 (32.1%)	31 (47.7%)	0.16
Two-VD	5 (35.7%)	4 (44.4%)	0.98	7 (25.0%)	17 (26.1%)	0.90
Three-VD	5 (35.7%)	0 (0%)	0.04	6 (21.4%)	12 (18.5%)	0.80
PCI procedure	10 (71.4%)	9 (100%)	0.08	21 (75.0%)	52 (80.0%)	0.59
Stent implantation	7 (50.0%)	6 (66.7%)	0.43	17 (60.7%)	41 (63.1%)	0.83

DM — diabetes mellitus; Cx - circumflex artery; LAD — left anterior descending artery; LMCA — left main coronary artery; RCA — right coronary artery; VD — vessel disease; PCI — percutaneous coronary intervention; TIMI — Thrombolysis In Myocardial Infarction; IRA — infarction related artery

were higher compared to normoglycaemic DM patients with STEMI (20.76  $\pm$  19.25 vs 1.74  $\pm$  0.89 ng/mL troponin I; p = 0.02) (Table 3).

During the in-hospital observation period the need for urgent CABG, repeated ACS occurrence, frequency of stroke or TIA, sudden cardiac arrest, all-cause death, repeated PCI procedure and LVEF value was similar in hyperglycaemic and normoglycaemic DM patients. The composite end-point was reached in 28.6% of hyperglycaemic and 11.2% of normoglycaemic DM patients (NS). Also during the four-year follow-up period (after index hospitalisation) the outcome of both subgroups was similar (Table 3).

# Subjects without diabetes mellitus

Of the 93 non-DM patients, 28 (30%) were classified as hyperglycaemic and 65 (70%) as normoglycaemic. A history of MI was more prevalent in the normoglycaemic group (Table 1). Hyperglycaemic and normoglycaemic non-DM patients had similar incidence of three-vessel CAD (21.4% vs 18.4%; NS), PCI procedure (75.0% vs 80.0%; NS) and TIMI 3 flow after PCI (100% vs 98.1%; NS) (Table 2).

During the in-hospital observation period, hyperglycaemic and normoglycaemic non-DM patients had similar incidence of urgent CABG, repeated ACS stroke or TIA, repeated PCI procedure and LVEF value. Sudden cardiac arrest occurred more frequently in hyperglycaemic subjects (3.6% vs 0.0%; n=1 vs 0; p=0.01). The composite end-point was reached in 17.6% of hyperglycaemic and 13.8% of normoglycaemic non-DM subjects (NS) (Table 3).

During the four-year follow-up period, hyperglycaemic and normoglycaemic non-DM patients had similar incidence

of all-cause death, repeated MI, PCI, CABG, stroke and TIA. However, hyperglycaemic subjects were more likely to reach the composite end-point than normoglycaemic subjects (78.6% vs 56.9%; p = 0.04).

During the four-year follow-up period, newly diagnosed DM was reported in 17% of hyperglycaemic patients and in 12% of normoglycaemic patients during the acute phase of ACS (NS) (Table 3).

# **DISCUSSION**

This four-year observational study found that hyperglycaemia in the acute phase of ACS was associated with a higher incidence of unfavourable cardiovascular (CV) events in non-DM patients, but did not influence CV outcomes in DM patients. Moreover, in hyperglycaemic non-DM patients, in-hospital sudden cardiac arrest was more frequent compared to normoglycaemic non-DM patients.

The mechanisms underlying the development of hyper-glycaemia in ACS patients remain inadequately understood. Acute hyperglycaemia is usually regarded as a reaction to stress, and in ACS, stress reaction is directed toward short-term optimisation of CV function. Other possible causes of acute hyperglycaemia are undiagnosed DM and glucose metabolism disorders, and although such chronic conditions can be managed, it may not be possible to normalise them in cases of severe disease and 'metabolic storm'. It may be that glycaemia on admission is not only a marker of acute stress, but also reflects the current metabolic status. Furthermore, the unfavourable effects of hyperglycaemia on the prognosis for ACS patients may result from intensification of inflammatory conditions [7].

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**Table 3.** Comparison of in-hospital parameters and long-term follow-up outcome between hyperglycaemic and normoglycaemic patients

	Patients wit	th DM (n = 23)		Patients without DM (n = 93)		
	Hyperglycaemia	Normoglycaemia	a P	Hyperglycaemia	Normoglycaemia	P
	N = 14 (61%)	N = 9 (39%)		N = 28 (30%)	N = 65 (70%)	
Max. troponin I concentration	on 19.53 ± 19.1	1.35 ± 1.07	0.02	14.8 ± 17.12	12.18 ± 16.18	0.56
all ACS types [ng/mL]	[9.55; 4.5–33]	[1.14; 0.1–2.25]		[4.2; 1.99–30]	[3.45; 0.28–15.9]	
[median; interquartile range	.]					
Max. CK concentration	1610 ± 1339	930 ± 1577	0.29	$2766 \pm 2981$	$1458 \pm 2509$	0.04
all ACS types [U/L]	[1234; 596–2437]	[324; 110.5–867.5]		[1499; 665–4713]	[535; 81–1403]	
[median; interquartile range	e]					
Max. troponin I concentration	$20.76 \pm 19.25$	$1.74\pm0.89$	0.02	$17.8 \pm 16.3$	$16.5 \pm 18.4$	0.70
STEMI patients [ng/mL] [median; interquartile range	[10.17; 6.31–33] e]	[1.52; 1.07–24.2]		[8.24; 3.02–33.5]	[8.09; 1.85–26.67]	
Max. CK concentration	$1706 \pm 1344$	$1652 \pm 2093$	0.96	$3066 \pm 3064$	$1953 \pm 2634$	0.09
STEMI patients [U/L] [median; interquartile range	[1403; 597–2437] e]	[86.75; 495–2820]		[1469; 695–4871]	[1931; 494–2260]	
SCA during hospitalisation	0 (0%)	0 (0%)	-	1 (3.6%)	0 (0%)	0.01
HF during hospitalisation	2 (14.3%)	0 (0%)	0.67	2 (7.1%)	1 (1.5%)	0.44
Stroke during hospitalisation	n 0 (0%)	0 (0%)	_	0 (0%)	0 (0%)	
Need for urgent CABG	2 (14.3%)	0 (0%)	0.36	3 (10.7%)	8 (12.3%)	0.89
Repeated PCI procedure during hospitalisation	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
Repeated ACS occurrence during hospitalisation	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
Ejection fraction [%]	48 ± 11.53	49 ± 10.8	0.86	$49.75 \pm 9.96$	$52.74 \pm 9.86$	
[median; interquartile range	e] [50; 37–65]	[48; 45–50]		[50; 45–57]	[54.5; 50–60]	
Time of hospitalisation (day:	s) 9.21 ± 6.13	$6.12 \pm 2.8$	0.19	$7.36 \pm 3.89$	$6.15 \pm 3.42$	0.16
[median; interquartile range	e] [7; 5–10]	[5.5; 4.5–7]		[7; 5–8]	[6; 4–7]	
In-hospital mortality	2 (14.3%)	1 (11.1%)	0.68	2 (7.1%)	1 (1.5%)	0.44
Composite end-point during in-hospital observation perio	•	1 (11.1%)	0.33	5 (17.9%)	9 (13.8%)	0.62
Mortality during follow-up per	riod 2 (14.3%)	1 (11.1%)	0.68	5 (17.9%)	7 (10.8%)	0.35
Repeated ACS occurrence during follow-up period	4 (28.6%)	1 (11.1%)	0.33	5 (17.9%)	9 (13.8%)	0.62
Repeated PCI procedure during follow-up period	3 (21.4%)	4 (44.4%)	0.48	7 (25%)	10 (15.4%)	0.27
CABG during follow-up peri	od 1 (7.1%)	0 (0%)	0.82	5 (17.9%)	9 (13.8%)	0.62
Stroke or TIA during follow-up period	1 (7.1%)	0 (0%)	0.82	1 (3.6%)	4 (6.1%)	0.96
Composite end-point	9 (64.3%)	6 (66.7%)	0.90	22 (78.6%)	37 (56.9%)	0.04
during follow-up period						
Newly diagnosed diabetes after hospital discharge	-	-	-	5 (17.9%)	8 (12.3%)	0.48

ACS — acute coronary syndrome; DM — diabetes mellitus; CABG — coronary artery bypass grafting; CK — creatine kinase; HF — heart failure; PCI — percutaneous coronary intervention; SCA — sudden cardiac arrest; TIA — transient ischaemic attack

Acute hyperglycaemia is associated with a higher risk of in-hospital complications in ACS patients, independent of a prior diagnosis of DM [2, 3, 8]. Some reports have suggested that this association results in a similar risk of complications in both DM and non-DM patients [3], although other authors reported the higher risk in non-DM patients [2, 9]. Studies examining the effects of acute hyperglycaemia on the long-term prognosis of ACS patients are limited, and have maximal follow-up of only three years [9, 10].

Similar findings to our study were presented by Monteiro et al. [9], who reported that increased glucose levels on admission were associated with higher mortality rates during both in-hospital and three-year follow-up in non-DM patients, but not in DM patients. In a one-year observational study of 1,310 STEMI patients (352 DM [26.9%] vs 958 non-DM [73.1%] patients), Gasior et al. [10] reported that increased glucose levels measured in the acute phase of MI affected the prognosis in non-DM patients, but was not an independent risk factor of death in DM patients treated with PCI. Ishihara et al. [11] found that hyperglycaemia on admission was a short--term risk factor in STEMI patients, but did not correlate with mortality during the period of 30 days to three years after MI. They also found that there was no association between DM and mortality during short-term follow-up, but that DM influenced the long-term prognosis. The apparent discrepancies between the findings of the various studies may reflect different glucose levels being used to define hyperglycaemia.

A precise and widely acceptable biochemical definition of acute hyperglycaemia has yet to be established. In studies evaluating the impact of acute hyperglycaemia on outcomes during ACS, the threshold level of hyperglycaemia has varied between 6.7 and 11.1 mmol/L (120–200 mg/dL) for admission glycaemia, and between 6.1 and 8.0 mmol/L (110–144 mg/dL) for the first fasting glucose level [11–14]. In our study, hyperglycaemia was defined as an admission glycaemia above 140 mg/dL (7.8 mmol/L) in DM patients and above 180 mg/dL (10.0 mmol/L) in non-DM patients, in accordance with the recommendations of the Polish Diabetes Association on hypoglycaemic treatment in states of "relative hyperglycaemia" [6].

We believe that using both admission and first fasting glycaemia measurements is crucial when classifying ACS patients as normoglycaemic or hyperglycaemic because it provides a more reliable and precise evaluation of the real state of carbohydrate metabolism compared to using either measurement alone. Indeed, others have reported that use of a single glucose measurement is not an optimal diagnostic tool for estimating carbohydrate metabolism [15, 16]. Although there are some doubts about the reliability of OGTT in diagnosing DM in ACS patients, reports from the GAMI Study on OGTT in MI [17] and the results of Swedish studies [18] suggest that OGTT is a reliable method of diagnosing glucose

metabolism disturbances in patients with ACS, but only when it is performed after the early phase of MI (fourth day or later).

We found that the glycaemic status did not affect in-hospital mortality or the long-term incidence of unfavourable CV events in DM patients. We found that there were no significant differences between the normo- and hyperglycaemic subgroups in the frequency of CV risk factors. These results are consistent with findings from the study by Kosiborod et al. [19], in which hyperglycaemia was found not to be associated with an increase in in-hospital or one-year mortality in ACS patients with DM, with the exception of patients with a glucose level > 240 mg/dL.

We found that three-vessel CAD was more common in DM than non-DM patients, and as a consequence, urgent CABG procedures were more often performed in hypergly-caemic DM patients. It is possible that hyperglycaemia in diabetics, as a marker of carbohydrate metabolism disturbance, might be a chronic state responsible for diffuse atherosclerotic changes developing in a younger age, and may lead to more frequent occurrence of three-vessel CAD.

In the current study, normoglycaemic and hyperglycaemic non-DM patients had comparable in-hospital mortality. However, normoglycaemic and hyperglycaemic non-DM patients differed in terms of the frequency of obesity and a history of prior MI. We found that hyperglycaemia in ACS patients with DM was associated with a larger area of myocardial necrosis (a difference in the level of myocardial necrosis markers was observed in the STEMI subgroup). These results are in accordance with those of the Global Registry of Acute Coronary Events (GRACE) which reported that higher levels of admission glycaemia were associated with increased MI size [5].

# Limitations of the study

This study was a retrospective pilot analysis of a relatively small number of patients treated in a single centre.

#### **CONCLUSIONS**

- Hyperglycaemia is an unfavourable long-term prognostic factor, and may also be an unfavourable factor during the in-hospital stay, in patients hospitalised due to ACS who are not diabetic.
- Hyperglycaemia does not appear to affect either the inhospital or four-year clinical outcomes in patients hospitalised due to ACS who are diabetic.

# Conflict of interest: none declared

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# Wpływ ostrej hiperglikemii na rokowanie wewnątrzszpitalne i długoterminowe u pacjentów z ostrymi zespołami wieńcowymi — badanie pilotażowe

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## Streszczenie

**Wstęp:** Ostra hiperglikemia jest niekorzystnym czynnikiem rokowniczym u pacjentów z ostrymi zespołami wieńcowymi (OZW). Istnieją rozbieżne dane dotyczące wpływu ostrej hiperglikemii na rokowanie w zależności od obecności lub braku rozpoznania cukrzycy.

**Cel:** Celem pracy była ocena wpływu ostrej hiperglikemii u chorych z OZW na rokowanie wewnątrzszpitalne i odległe (obserwacja 4-letnia) u pacjentów bez cukrzycy i u chorych z rozpoznaną cukrzycą.

**Metody:** U 116 pacjentów hospitalizowanych w latach 2004–2006 w I Klinice Kardiologii i Nadciśnienia Tętniczego Szpitala Uniwersyteckiego w Krakowie z powodu OZW, zakwalifikowanych do pilnej diagnostyki inwazyjnej choroby niedokrwiennej serca, oznaczano stężenie glukozy w krwi żylnej w chwili przyjęcia do szpitala oraz następnego dnia na czczo. Chorych podzielono na dwie grupy: z rozpoznaną cukrzycą (przed epizodem OZW lub w trakcie hospitalizacji) oraz bez cukrzycy, wyodrębniając w obu grupach osoby z hiperglikemią i normoglikemią. Ostrą hiperglikemię definiowano jako stężenie glukozy przy przyjęciu ≥ 10,0 mmol/l (180 mg/dl) w grupie osób bez cukrzycy, w grupie pacjentów z cukrzycą ≥ 7,8 mmol/l (140 mg/dl) lub pierwszą glikemię na czczo ≥ 5,6 mmol/l (100 mg/dl) (w obu grupach). Ostrą hiperglikemię stwierdzono u 14 chorych na cukrzycę oraz u 28 pacjentów bez cukrzycy. Średni czas obserwacji wynosił 4 ± 0,6 roku. Za pierwotny punkt końcowy przyjęto śmiertelność 4-letnią. Wtórne punkty końcowe stanowiły: zgon, nagłe zatrzymanie krążenia, ponowny zawał serca, udar mózgu lub przejściowy epizod niedokrwienny mózgu (TIA), konieczność pilnego zabiegu pomostowania aortalnowieńcowego (CABG) lub powtórnej angioplastyki (PCI) w obserwacji wewnątrzszpitalnej i 4-letniej. Złożony punkt końcowy w obserwacji wewnątrzszpitalnej i 4-letniej zdefiniowano jako wystąpienie co najmniej 1 zdarzenia spośród: zgonu z jakiegokolwiek powodu, ponownego zawału serca, udaru mózgu, konieczności powtórnej PCI lub CABG.

**Wyniki:** U pacjentów z cukrzycą śmiertelność 4-letnia nie różniła się istotnie między grupą chorych z hiperglikemią i normoglikemią (14,3% v. 11,1%; p = NS). Wtórne punkty końcowe i złożony punkt końcowy w tej grupie pacjentów wystąpił z podobną częstością w podgrupie z hiperglikemią i normoglikemią, zarówno w okresie wewnątrzszpitalnym, jak i w trakcie 4-letniej obserwacji. Wśród pacjentów bez cukrzycy śmiertelność 4-letnia również nie różniła się istotnie w podgrupie z hiperglikemią i normoglikemią (17,9% v. 10,8%; p = NS). U chorych z hiperglikemią istotnie częściej dochodziło do nagłego zatrzymania krążenia w trakcie pobytu w szpitalu (3,6% v. 0,0%; n: 1 v. 0; p = 0,01). Złożony punkt końcowy w obserwacji wewnątrzszpitalnej wystąpił u 17,6% osób z hiperglikemią i u 13,8% osób z normoglikemią (p = NS). Złożony punkt końcowy w obserwacji 4-letniej stwierdzono istotnie częściej w podgrupie z hiperglikemią w porównaniu z pacjentami z normoglikemią (78,6% v. 56,9%; p = 0,04).

**Wnioski:** U osób bez cukrzycy hospitalizowanych z powodu OZW hiperglikemia stanowi niekorzystny czynnik rokowniczy w obserwacji długoterminowej, może też być niekorzystnym czynnikiem rokowniczym w obserwacji wewnątrzszpitalnej. Ostra hiperglikemia u chorych na cukrzycę hospitalizowanych z powodu OZW nie wpływa na częstość zdarzeń sercowonaczyniowych w obserwacji wewnątrzszpitalnej i 4-letniej.

Słowa kluczowe: cukrzyca, hiperglikemia, ostry zespół wieńcowy, czynnik ryzyka

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