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Abstract

Some studies of patients with acute myocardial infarction have reported that hyperglycaemia at admission may be associated with a worse outcome. This study sought to evaluate the association of blood glucose at admission with the outcome of unselected patients with acute coronary syndrome (ACS).

Using the Acute Myocardial Infarction and unstable angina in Switzerland (AMIS Plus) registry, ACS patients were stratified according to their blood glucose on admission: group 1: 2.80–6.99 mmol/L, group 2: 7.00–11.09 mmol/L and group 3: ≥ 11.10 mmol/L. Odds ratios for in-hospital mortality were calculated using logistic regression models.

Of 2,786 patients, 73% were male and 21% were known to have diabetes. In-hospital mortality increased from 3% in group 1 to 7% in group 2 and to 15% in group 3. Higher glucose levels were associated with larger enzymatic infarct sizes (p<0.001) and had a weak negative correlation with angiographic or echographic left ventricular ejection fraction. High admission glycaemia in ACS patients remains a significant independent predictor of in-hospital mortality (adjusted OR 1.08; 95% confidence intervals [CI] 1.05–1.14, p<0.001) per mmol/L. The OR for in-hospital mortality was 1.04 (95% CI 0.99–1.1; p=0.140) per mmol/L for patients with diabetes but 1.21 (95% CI 112–1.30; p<0.001) per mmol/L for non-diabetic patients.

In conclusion, elevated glucose level in ACS patients on admission is a significant independent predictor of in-hospital mortality and is even more important for patients who do not have known diabetes.

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Key words: acute coronary syndrome, admission glycaemia, diabetes, gender, hyperglycaemia, outcome.

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Introduction

Diabetes mellitus is associated with an increased risk of cardiovascular morbidity and mortality.[1,2] Findings of a meta-regression analysis suggest that even blood glucose levels below the threshold for diabetes are related to raised cardiovascular risk.[3] Patients with a longer duration of diabetes more frequently show signs of diabetic neuropathy that can result in atypical symptoms during myocardial infarction. Thus, diagnosis of an acute coronary syndrome (ACS) is more difficult in these patients and initiation of adequate therapy is often delayed.[4] Among patients with acute myocardial infarction (AMI), diabetes mellitus is associated with higher mortality rates, both in-hospital[5,6] and during long-term follow-up.[5,7] This is the case across the whole spectrum of ACS.[8] In that study, ACS patients with diabetes had a higher risk of both death and re-infarction at 30 days than those without diabetes, and the rates of death or re-infarction at six months remained higher in the diabetic group, whether they presented with ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI).

High blood glucose levels in patients admitted for ACS/AMI are common and are associated with an increased risk of death in both patients with diabetes[9-19] and patients without diabetes.[9-17,19] Admission hyperglycaemia is an even stronger predictor for mortality in patients without a medical history of diabetes.[9,13,19]

However, there is little information about differences in outcome between men and women with hyperglycaemia on admission for ACS/AMI. The aim of our study was to investigate the association of admission glycaemia and outcome in

Table 1. Baseline characteristics and outcome of all ACS patients according to admission glycaemia groups

Glucose levels (mmol/L)	G1: 2.80–6.99	G2: 7.00–11.09	G3: ≥ 11.10	p values
Number of patients (n=2,786)	**1,299**	**1,117**	**370**	
Glycaemia on admission (mmol/L)				
mean (SD)	5.9 (0.7)	8.4 (1.1)	15.4 (4.5)	0.001
median	6.0	8.2	13.7	
Age min - max	28–95	27–96	37–93	0.01
mean ± SD	65 (13)	67 (13)	69±13	
median	65	68	71	
Sex male (%)	993/1,299 (76.4)	795/1,117 (71.2)	252/370 (68.1)	
female (%)	306/1,299 (23.6)	322/1,117 (28.8)	118/370 (31.9)	0.001
Past medical history				
Hypertension (%)	728/1,259 (57.8)	661/1,074 (61.5)	267/354 (75.4)	<0.001
Dyslipidaemia (%)	679/1,162 (58.4)	567/991 (57.2)	206/332 (62.0)	0.306
Smoking (current) (%)	477/1,246 (38.3)	342/1,042 (32.8)	106/329 (32.2)	0.011
Obesity (BMI ≥ 30 kg/m²) (%)	194/1,151 (16.9)	219/999 (21.9)	83/305 (27.2)	<0.001
Co-morbidities				
Moderate-to-severe renal disease (%)	72/1,273 (5.7)	95/1,080 (8.8)	50/362 (13.8)	<0.001
Diabetes (%)	114/1,299 (8.8)	215/1,117 (19.2)	244/370 (65.9)	<0.001
Delay in minutes (median, interquartile range)	255 (120, 810) (n=1,007)	210 (110, 600) (n=926)	210 (103, 770) (n=278)	0.013
CPR (%)	10/1,251 (0.8)	17/1,076 (1.6)	32/347 (9.2)	<0.001
Killip class III/IV (%)	24/1,297 (1.9)	53/1,109 (4.8)	63/365 (17.3)	<0.001
Symptoms on admission				
Atypical (%)	136/1,277 (10.6)	145/1,097 (13.2)	75/359 (20.9)	<0.001
STEMI (%)	615/1,298 (47.4)	689/1,117 (61.7)	215/370 (58.1)	<0.001
Angiographic findings				
Three-vessel disease (%)	300/985 (30.5)	277/848 (32.7)	89/230 (38.7)	0.053
Insulin (during initial treatment) (%)	93/1,277 (7.3)	176/1,084 (16.2)	208/364 (57.1)	<0.001
Reperfusion				<0.001
Thrombolysis (%)	40/1,281 (3.1)	42/1,110 (3.8)	9/369 (2.4)	
PCI primary (%)	772/1,281 (60.3)	729/1,110 (65.7)	188/369 (50.9)	
Outcome				
MACE	4.9	10.1	18.7	<0.001
In-hospital mortality	2.6	7.3	14.9	<0.001

Key: CPR = cardiopulmonary resuscitation; STEMI = ST segment elevation myocardial infarction; PCI = percutaneous coronary intervention; MACE = major adverse cardiac events; BMI = body mass index

patients admitted for ACS; furthermore, to examine if there are differences in outcome not only between patients with and without diabetes, but also between men and women with hyperglycaemia at hospital admission.

Patients and methods

The AMIS Plus Registry

In 1997, the Swiss Societies of Cardiology, Internal Medicine and Intensive Care initiated a nationwide prospective registry to assess the diagnostic and therapeutic measures for patients with AMI in Switzerland (AMIS). Academic and non-academic hospitals participate voluntarily and provide blinded data on these patients to the AMIS Plus Data Center through an internet- or paper-based questionnaire of 140 questions. The Data Center controls and checks the data for plausibility and cross-checks in case of queries. In the year 2000, patients with unstable angina were added to the registry. AMIS Plus is an industry-sponsored project, but the supporting institutions do not play any role in the design of the registry, data collection, analysis or interpretation. The project is led by a Steering Committee comprised of members of the founding societies. The registry was approved by the Over-regional Ethical Committee for Clinical Studies and the Swiss Board of Data Security.[20,21] In March 2005 the AMIS Plus Questionnaire was revised and admission glycaemia was included.

Patients

Patients enrolled in the AMIS Plus registry from March 2005 to March 2006 across the whole spectrum of ACS and with valid data both on glycaemia at admission and history of diabetes were included. The spectrum covered AMI, defined by characteristic symptoms and/or ECG changes and enzymes (total creatine kinase [CK] or creatine kinase MB fraction greater than twice the upper limit of normal), minimal necrosis (the same, but the enzymes below twice the

Table 2. Predictors of in-hospital mortality at admission by logistic regression analysis in patients with ACS (n=2,525)

	Odds ratio	95% CI	Significance
Glucose levels per mmol/L	1.08	1.05–1.14	0.001
Age per year	1.07	1.05–1.10	<0.001
Gender	0.84	0.55–1.27	0.399
History of diabetes	0.86	0.53–1.39	0.545
History of arterial hypertension	0.89	0.72–1.75	0.602
Renal disease	2.23	1.38–3.62	0.001
Killip class II	1.57	0.99–2.49	0.056
Killip class III	1.83	0.88–3.82	0.106
Killip class IV	6.11	2.73–13.65	<0.001
STEMI	1.78	1.19–2.66	0.005
CPR	6.49	2.88–14.61	<0.001
Heart rate	1.00	0.99–1.01	0.553
Systolic blood pressure	0.98	0.97–0.99	<0.001
Percutaneous coronary intervention	0.47	0.30–0.75	0.002

Key: CI = confidence intervals; ACS = acute coronary syndromes; STEMI = ST segment elevation myocardial infarction; CPR = cardiopulmonary resuscitation

upper limit of normal and troponin-positive) and unstable angina (symptoms and/or ECG typical for ACS, normal enzymes). Patients were defined as diabetic when diabetes mellitus was reported in their past medical history, independent of the kind of treatment they were receiving (oral agents, insulin-treated or untreated). Co-morbidities were documented using the Charlson Comorbidity Index.[22] Other risk factors previously diagnosed, treated and/or documented in the patients' medical history were also identified. Patients were stratified into three admission glycaemia groups: normal (G1: 2.80–6.99 mmol/L), intermediate (G2: 7.00–11.09 mmol/L) and elevated glucose concentrations (G3: ≥ 11.10 mmol/L). Baseline characteristics and outcome were compared between these three groups. Within G3 we compared short-term outcome of diabetic versus non-diabetic patients and of male versus female ACS patients. The end point was set as major adverse cardiac events (MACE), including re-infarction, stroke and death or in-hospital mortality.

Statistical analyses

Data are presented as percentages for discrete variables and as means (SD) and/or medians with interquartile range for continuous variables. Differences in baseline characteristics were compared using the *t*-test and the chi-squared test. A p value <0.05 was considered statistically significant.

Logistic regression models for predicting in-hospital mortality were conducted using the Enter method with the following variables: age, gender, history of diabetes mellitus, hypertension and renal disease, cardiopulmonary resuscitation (CPR), Killip class, STEMI, systolic blood pressure, heart rate on admission and primary percutaneous coronary intervention (PCI).

SPSS (Chicago, III, US) for Windows XP (version 13.0) was used for all statistical analyses.

Results

Overall patient population

Of 2,924 ACS patients, 2,790 cases met the inclusion criteria. Four patients with hypoglycaemia at admission (< 2.80 mmol/L) were excluded because the numbers were so small. Of the remaining 2,786 cases, 2,040 (73%) were male and 746 (27%) female, 573 (21%) were known to have diabetes and 2,213 (79%) were non-diabetic or their diabetes status was unknown.

At hospital admission, the majority of ACS patients (47%) had normal glucose levels (2.80–6.99 mmol/L, G1), 40% intermediate levels (7.00–11.09 mmol/L, G2) and 13% had clearly elevated glucose levels (≥ 11.10 mmol/L, G3). Patient characteristics for the three groups are shown in table 1. Patients with increased glucose levels were more often diabetic. They were older, more likely to be female and obese, and more often had a past medical history of arterial hypertension and moderate-to-severe renal disease. The frequencies of a past medical history of dyslipidaemia were similar in all three groups. The delay from onset of symptoms to hospitalisation tended to be longest in G1. Patients in G3 needed CPR more often prior to arrival at hospital, and presented more often with Killip classes III/IV and atypical symptoms compared to G1 and G2, respectively. Patients in G2 and G3 suffered a STEMI more often than patients in G1. Those in G1 were more likely to be current smokers. There was a tendency towards a greater number of patients with

three-vessel disease in G3. G3 patients also received insulin within 24 hours of admission more often compared to G1 and G2, respectively. G3 patients experienced more strokes and cardiogenic shocks, whereas the frequencies of re-infarction were similar in the three groups. The major adverse cardiac events (MACE) rate was higher in G2 (10%) and G3 (19%) compared with G1 (5%). Overall in-hospital mortality was 6%, with differences among the groups: 3% in G1, 7% in G2 and 15% in G3.

Diabetics versus non-diabetics

Overall in-hospital mortality was 10% in all diabetic patients and 5% in all non-diabetic patients (p<0.001). Of the patients with admission glycaemia ≥ 11.10 mmol/L, 66% had a previous diagnosis of diabetes and 34% did not. In this hyperglycaemic group (G3), patients with previously diagnosed diabetes were older (70±12 *vs.* 68±14 years; p<0.001), had significantly more risk factors such as arterial hypertension (84% *vs.* 59%, p<0.001), dyslipidaemia (72% *vs.* 45%, p<0.001) and obesity (32% *vs.* 18%, p=0.009), but tended to be current smokers less often than non-diabetic patients (29% *vs.* 39%, p=0.0065). Diabetic patients were more often found to have three-vessel coronary artery disease (45% *vs.* 27%, p=0.007) and previous coronary artery bypass grafting (CABG; 9% *vs.* 3%, p=0.034) than non-diabetics.

The delay from onset of symptoms to hospitalisation was longer in diabetic than in non-diabetic patients (270 minutes; interquartile range 115–810 *vs.* 180 minutes; interquartile range 97–379 minutes, p=0.044), but there was no difference in the frequency of atypical symptoms on admission. Non-diabetics needed CPR significantly more often prior to arrival at hospital (14% *vs.* 7%, p=0.030). They tended to experience a STEMI more often (65% *vs.* 55%, p=0.096) and to be admitted in heart failure Killip class III/IV (23% *vs.* 15%, p=0.058). Reperfusion rates (thrombolysis and primary percutaneous coronary intervention; PCI) were similar, but patients without diabetes received insulin significantly less frequently as part of the initial treatment compared to patients with diabetes (29% *vs.* 72%, p=<0.001). In patients without diabetes, the hospital course was complicated more often by cardiogenic shock than in patients with diabetes (15% *vs.* 7%; p=0.020). The frequency of re-infarction and cerebrovascular insult was similar between diabetic and non-diabetic patients. Non-diabetics with admission glycaemia ≥ 11.10 mmol/L had a non-significantly higher MACE rate (25% *vs.* 16%; p=0.053) and in-hospital mortality (20% *vs.* 12%; p=0.064) compared to diabetic patients.

Female versus male patients

Overall, in-hospital mortality was 6% in all men and 8% in all women (p=0.075). Of the patients with admission glycaemia ≥ 11.10 mmol/L, 252 (68%) were male and 118 (32%) female. The mean glucose levels were similar in both genders (15.3 mmol/L *vs.* 15.5 mmol/L, p=0.821) while male patients were on average eight years younger than female patients (67 *vs.* 75 years, p<0.001). Frequency of history of diabetes was similar in both genders (65% *vs.* 69%, p=0.482) while female patients tended to have moderate-to-severe renal disease more often (19% *vs.* 12%, p=0.074). Males had significantly less arterial hypertension (70% *vs.* 86%, p=0.001) as a risk factor, but were more often current smokers (40% *vs.* 15%, p<0.001) and overweight (77% *vs.* 60%, p=0.004) and more frequently had a history of CABG (10% *vs.* 2%, p=0.004). The proportion with a history of dyslipidaemia (63% *vs.* 59%, p=0.541) was similar in both genders. In females, the delay from onset of symptoms to hospitalisation was about twice as long as in males (358 minutes; interquartile range 120–939 minutes *vs.* 180 minutes; interquartile range 96–642 minutes, p<0.001), and they tended to have atypical symptoms more often (27% *vs.* 18%, p=0.071) on admission. Male patients tended to present more often with STEMI (61% *vs.* 52%, p=0.091) and needed CPR significantly more frequently prior to arrival at hospital (13% *vs.* 2%, p=0.001). Heart failure on admission (Killip class III/IV) and complications (cardiogenic shock, re-infarction and cerebrovascular insult) were, however, similar in both male and female patients. Although males received insulin significantly more often as immediate medication (61% *vs.* 49%, p=0.031) and underwent primary PCI more frequently (57% *vs.* 39%, p=0.10), they had a significantly worse outcome. Male patients had a higher MACE rate (23% *vs.* 11%; p=0.014) and higher in-hospital mortality (18% *vs.* 8%; p=0.007) than females.

Glucose levels and infarct size

There was a highly significant, but weak, positive correlation between glucose levels and maximum CK levels during hospitalisation (n=2,747, correlation coefficient 0.18, p<0.001), a weak negative correlation between glucose levels and angiographic left ventricular ejection fraction (LVEF; n=1,684, correlation coefficient -0.16, p<0.001) and a weak negative correlation between glucose levels at admission and echographic LVEF (n=1,084, correlation coefficient -0.27, p<0.001).

Predictors of in-hospital mortality at admission by logistic regression analysis in ACS patients

In multivariate logistic regression analysis, higher admission glycaemia remained an independent predictor of in-hospital mortality (table 2). The unadjusted OR for in-hospital mortality for glucose levels was 1.14 (95% CI 1.12–1.18) per mmol/L, and adjusted OR was 1.08 (95% CI 1.05–1.14, p<0.001). The OR for in-hospital mortality was 1.04 (0.99–1.1; p=0.140) per mmol/L for diabetic patients but 1.21 (112–1.30; p<0.001) per mmol/L for non-diabetic patients; and 1.07 (0.97–1.15; p=0.109) for female patients and 1.11 (1.05–1.17; p<0.001) for male patients.

Discussion

The results of this study showed that patients presenting with an ACS who are hyperglycaemic on admission represent a high-risk population, even in the absence of an established diagnosis of diabetes. Abnormal glucose metabolism during the acute phase of AMI or ACS is common, and admission hyperglycaemia is associated with increased short-term mortality in both diabetic[11-13,17-19] and non-diabetic[11-13,17,19] patients. Moreover, short-term mortality is predicted even more

powerfully by admission hyperglycaemia in patients without known diabetes.[13,19]

In-hospital mortality rates of all ACS patients in G1 (3%), G2 (7%), and G3 (15%) in our study are in line with those from another study that investigated the association of glycaemia on admission and outcome in patients admitted for AMI (< 7.8 mmol/L: 1%, 7.8–11 mmol/L: 6%, > 11 mmol/L: 17%).[17] Further, in-hospital mortality rates of diabetic (12%) and non-diabetic patients (20%) in G3 are similar to those observed by Wahab[19] (diabetic > 11 mmol/L: 19%; non-diabetic > 11 mmol/L: 24%).

In our study, increased glucose levels at admission in ACS patients were associated with an increase of in-hospital mortality of 8% per mmol/L, even after adjustment for covariables. The impact of an elevated admission glucose level on in-hospital mortality was even more important for non-diabetic than for diabetic ACS patients (interaction between glucose levels and history of diabetes OR=0.87;95% CI 0.79–0.94). Similarly, 30-day mortality was predicted by baseline glucose with a hazard ratio of 1.12 per 0.6 mmol/L increase in patients without diabetes, but not in those with diabetes.[13] In addition, several studies have shown that hyperglycaemia on admission is associated with long-term mortality after AMI or ACS in both patients with[9,10,13-19] and without[9,10,13-17,19] previously known diabetes.

There are several possible causes of hyperglycaemia on admission in patients with ACS, but it is not clear why it should be associated with poor outcome. First, hyperglycaemia on admission in non-diabetic ACS patients might represent previously undiagnosed diabetes or pre-existing impaired glucose tolerance. Wahab[19] suggested that in non-diabetic AMI patients, hyperglycaemia probably represents unrecognised and therefore untreated diabetes, with many years of uncontrolled elevated blood glucose levels resulting in increased endothelial damage and thus greater risk for macro- and micro-vascular morbidity. However, Tenerz[23] found that in non-diabetic patients with AMI, increased blood glucose on admission was not a reliable method of establishing a diagnosis of diabetes and follow-up was necessary. Nevertheless, a substantial proportion of the non-diabetic patients with even only slightly elevated admission glycaemia (< 11.10 mmol/L) have undiagnosed diabetes or impaired glucose tolerance,[24] thus bearing an increased risk of poor outcome after AMI/ACS.[5-8]

Secondly, hyperglycaemia on admission in ACS patients might represent a response to acute and severe stress[11] whereas increased catecholamine levels result in decreased insulin secretion and increased insulin resistance. In the CARDINAL study,[13] individuals with higher baseline glucose (upon diagnosis of AMI) had larger infarct sizes, determined by CK-MB area under the curve. In the Zwolle trial[25] there was a clear association between LVEF, measured by equilibrium radionuclide ventriculography, and glucose levels in non-diabetic patients with myocardial infarction. Higher glucose levels on admission were correlated with lower LVEF. These findings suggest that high glucose levels on admission might be a marker of large myocardial infarctions and therefore also reflect severe stress and a high risk of poor prognosis. In our study, there was a significant positive correlation between glucose levels and infarct size, measured as maximum CK, and a negative correlation between glucose levels and LVEF measured on angiography and echocardiography.

In the DIGAMI study,[14] glycosylated haemoglobin, body weight, heart rate and pulmonary rales on admission were independently linked to admission hyperglycaemia. These factors might reflect both previously unrecognised diabetes and severe stress during the acute phase of AMI.

In this study, CPR prior to arrival at hospital might have played an important role in the clinical course of ACS. Of all ACS patients, the highest frequencies of CPR were found in G3 (in non-diabetics and in males). Hyperglycaemia in these patients could have been a result of CPR and would therefore represent severe stress. However, it is also possible that hyperglycaemia itself led to a worse clinical course and cardiac arrest in the acute phase of ACS, necessitating CPR. Since autonomic neuropathy in diabetic patients may mask ACS, a larger proportion of hyperglycaemic diabetic patients than hyperglycaemic patients without diabetes might have died at home. However, if a high proportion of non-diabetic hyperglycaemic patients were in fact undiagnosed (and therefore untreated) diabetic patients, this might explain why they needed CPR significantly more often prior to arrival at hospital and why their hospital course was complicated more often by cardiogenic shock. It remains unclear whether hyperglycaemia is simply a marker of stress and of poor prognosis or whether hyperglycaemia predisposes to a worse outcome.[9]

In view of all these results, admission hyperglycaemia in non-diabetics during the acute phase of ACS and its association with poor outcome represents most likely a combination of previously undiagnosed diabetes, impaired glucose tolerance, and a response to acute and severe stress.[11]

In ACS, STEMI has a higher mortality rate than NSTEMI. In our study, patients with intermediate and high glucose levels presented more often with STEMI than NSTEMI, and non-diabetic males in G3 had the highest rate of STEMI, which could have contributed to their poor outcome. Outcome in STEMI is improved by reperfusion therapy, with a significant benefit for primary PCI over fibrinolysis.[13,26-28] In this study, patients in G3 received primary PCI significantly less frequently than those in G1 and G2, which might have contributed to the worse outcome in this group. These findings are in accordance with those of Straumann,[17] who found that in patients treated with PCI during the first 24 hours of an AMI, glucose levels > 11.0 mmol/L were a strong predictor of 30-day mortality even after adjustment for age, cardiogenic shock (Killip class IV), and TIMI 3 flow after PCI. There was no evidence of a different effect of glucose levels on survival between patients with and without cardiogenic shock (Killip class IV) on admission.

The DIGAMI study showed that immediate insulin-glucose infusion followed by multi-dose subcutaneous insulin reduced one-year mortality significantly in patients with AMI and admission blood glucose concentrations > 11.0 mmol/L, although the effect of this treatment on in-hospital mortality was not significant.[29] The second DIGAMI study did not support this. However, compared to the first DIGAMI trial, overall long-term glucose control was better in the second

DIGAMI trial, which may have had a favourable influence on outcome in the latter.[30]

Published risk score models for ACS to identify patients at high risk for death and other major cardiac ischaemic events have included a medical history of diabetes as a categorical variable.[31,32] Straumann[17] has stated that the categorical variable 'elevated admission blood glucose level' would be a more powerful predictor of outcome than the variable 'medical history of diabetes' in a modified risk score for patients with ACS.

There is little published information on the differences in outcome between men and women with hyperglycaemia at the time of admission for ACS. In the DIGAMI study, there was no significant difference in long-term mortality between male and female patients admitted for AMI with glycaemia $\geq$ 11.0 mmol/L, and female sex was not an independent, unfavourable prognostic factor.[15] In our study, overall in-hospital mortality tended to be higher in women than in men ($p=0.075$), while among the patients with admission glycaemia > 11.10 mmol/L, the MACE rate and in-hospital mortality were significantly higher in men than in women, even though men received primary PCI and insulin significantly more often as immediate medication, and women were older and had a history of hypertension more frequently. In males, but not in females, increased glucose levels at admission were associated with significant increases of in-hospital mortality of 11% per mmol/L even after adjusting for covariables. However, gender was not an independent predictor of in-hospital mortality in multivariate logistic regression analysis.

Detection of high-risk patients by applying reliable screening methods to all patients at admission for ACS is indispensable in order to ensure rapid and appropriate treatment and, consequently, decreased in-hospital mortality. Our study has shown that hyperglycaemia on admission is a strong risk factor for worse outcome in all patients admitted with ACS. Measurement of glycaemia at hospital admission may therefore be used as an early screening method to detect high-risk patients. Blood glucose concentrations are available within minutes of presentation, at a time when other elements of risk prediction models such as elevated serum markers of myocardial necrosis[17,31,32] may still be normal. According to diabetes guidelines, all patients with coronary artery disease and unknown diabetes status should be screened for type 2 diabetes by an oral glucose tolerance test (OGTT) that gives both fasting and two-hour post-load glucose values, and by measuring HbA_{1C}.[33] In patients admitted for ACS with significantly elevated blood glucose levels, normoglycaemia should be aimed for as soon as possible by means of insulin infusion.

Glucose levels at admission for ACS could therefore be used in order to detect high-risk individuals and to treat them adequately. In order to detect diabetes or impaired glucose homeostasis and therefore to prevent re-infarction or death during follow-up, these screening methods could be applied at discharge.

Study limitations

Differences in the use of drugs (aspirin, statins, β-blockers and angiotensin-converting enzyme [ACE] inhibitors) are known to influence the outcome of acute myocardial infarction and might have played a role in the effect on MACE and the in-hospital mortality rate.[34] In this study, we did not analyse the influence of these drugs on MACE or on the in-hospital mortality rate.

Since we did not measure HbA_{1C} at admission or fasting glucose after recovery, we were unable to tell whether hyperglycaemia at admission was caused by previously undiagnosed diabetes or by severe stress during the acute phase of ACS. We used the medical history to determine a previous diagnosis of diabetes mellitus, thus it is likely that some 'non-diabetics' had unrecognised diabetes mellitus.

It has recently been shown that there is a U-shaped relationship between admission blood glucose levels and poor outcome after STEMI; moderate and severe hyperglycaemia, and also hypoglycaemia, are associated with increased 30-day mortality, irrespective of history of diabetes.[35] Due to the small number of hypoglycaemic patients in our study, we were not able to verify a U-shaped relationship between admission glycaemia and adverse outcome after ACS.

In conclusion, the data from this study have shown that hyperglycaemia at admission is associated with a worse outcome for all patients admitted with ACS. Complications in general, cardiogenic shock, cerebrovascular insult and in-hospital mortality increased with higher levels of blood glucose. An elevated glucose level in ACS patients on admission remained a significant independent predictor of in-hospital mortality after adjustment for multiple risk factors known to be associated with increased in-hospital mortality. The impact of a higher admission glucose level on in-hospital mortality was even more important for non-diabetic than for diabetic ACS patients. Thus, non-diabetic patients with hyperglycaemia at admission were at special risk. They may need particular attention at hospital admission, therefore more aggressive screening strategies should be applied to all ACS patients in order to recognise these high-risk patients. According to our results, hyperglycaemia on admission clearly predicts a worse outcome and could therefore be used as an early marker of high-risk individuals. These patients may benefit from an appropriate treatment strategy, including strict glycaemic control. Further studies to evaluate the effect of acute and intensive glycaemic control on reducing in-hospital mortality in patients admitted for ACS are needed.

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Conflicts of interest statement

None declared.

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