Hemoglobin A1c as a prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction

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Objectives **We sought to determine the effect of hemoglobin A1c (HbA1c) on the outcomes of primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).**

Background **Diabetes mellitus (DM) can be diagnosed from a level of at least 6.5% on two separate occasions according to the American Diabetes Association (ADA) definition, which was updated in 2010. No data are available for the value of HbA1c in patients with STEMI treated with primary PCI.**

Methods **A total of 374 consecutive patients with STEMI (mean age: 55.9 ± 12.6 years, 318 men), undergoing primary PCI between December 2009 and June 2010, were prospectively enrolled in this study. Blood samples for HbA1c were obtained on the first 24 h after admission. In-hospital follow-up was performed. By using new ADA criteria, patients were classified into three groups: group I (HbA1c $\leq$ 5.6%, $n=112$); group II (HbA1c: 5.7–6.4%, $n=180$); and group III (HbA1c $\geq$ 6.5%, $n=82$).**

Results **In-hospital mortality was higher in group III (11%) compared with group II (2.8%) and group I (0.9%; $P=0.001$). Major adverse cardiac events in the hospital were also higher in group III (12.2%) compared with other groups (group II, 5.6% vs. group I, 0.9%, $P=0.003$). After adjusting the baseline characteristics, HbA1c remained a strong independent predictor of the in-hospital mortality (odds ratio: 1.412; 95% confidence interval: 1.031–1.935, $P=0.03$). Hospital stay was also longer in group III than others ($P=0.007$). A total of 196 (63.6%) patients without a history of diabetes mellitus had elevated HbA1c of more than or equal to 5.7%, with 31 (10.1%) of them having HbA1c of more than or equal to 6.5%.**

Conclusion **HbA1c is an independent predictor of the in-hospital mortality in STEMI treated with primary PCI. Apart from prognostic value, high HbA1c could be used for diabetes mellitus diagnosis, which is supported by ADA definitions.** *Coron Artery Dis* **22:131–137 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Diabetes mellitus (DM) is a chronic illness, and is associated with an increased risk of mortality after ST-segment elevation myocardial infarction (STEMI) [1]. It requires complex continuing medical care. For this reason, standards of care are revised annually by the American Diabetes Association (ADA). In the 2010 update, the ADA recommended the use of hemoglobin A1c (HbA1c) test to diagnose DM with a threshold of more than or equal to 6.5%. But the test should be certified by the National Glycohemoglobin Standardization Program and standardized to the Diabetes Control and Complications Trial reference assay. In addition, an HbA1c range of 5.7–6.4% should be considered as a high risk for future DM. The term 'prediabetes' may be used for this group [2].

HbA1c reflects the average blood glucose concentrations over the preceding 2–3 months [3]. There are advantages of HbA1c testing compared with glucose. The measurement of HbA1c is well standardized, and the biologic variability is less, and does not require fasting. In addition, it is relatively unaffected by acute changes in glucose levels [2].

Some evidences have shown that HbA1c levels may be of prognostic value with regard to future cardiovascular disease [4,5]. But there are divergent report results on the prognostic influence of HbA1c after STEMI with heterogene-analyzed groups. Thus, we decided to determine the effect of HbA1c by new ADA criteria on the outcomes of primary percutaneous coronary intervention (PCI) for STEMI.

Methods

Patient population

We prospectively evaluated 374 consecutive patients with STEMI who were admitted to the emergency department of

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our hospital and underwent urgent cardiac catheterization procedures between December 2009 and June 2010. Patients were enrolled in the study if they fulfilled the following criteria: (i) presenting within 12 h from the onset of symptoms (typical chest pain lasting for > 30 min); (ii) ST-segment elevation of more than or equal to 2 mm in at least two contiguous electrocardiogram leads or new onset of complete left bundle-branch block; (iii) treatment with primary PCI (angioplasty and/or stent deployment). Exclusion criteria were: no indication for PCI, treated with coronary bypass surgery (i.e. not suitable for PCI), and missing or unavailable data about HbA1c. All primary PCI procedures were performed in a single high-volume tertiary center (> 3000 PCI/year) by expert operators performing more than 75 PCIs per year. The study protocol was approved by the hospital's Ethics Committee.

Data sources

Demographic information and the clinical history of risk factors such as age, sex, DM, hypertension, hypercholesterolemia, smoking, family history for coronary artery disease (CAD), myocardial infarction history, PCI or bypass history, and earlier drug use were determined from patients and medical records. Angina-to-reperfusion time and door-to-balloon time, heart rate, blood pressure, and body mass index were calculated. Physical examination was done as well.

Blood values were determined at hospital admission (before catheterization procedures) and on a daily basis during the hospital stay. Blood samples for HbA1c were obtained on the first 24 h after admission. HbA1c was estimated using the Tina-Quant II turbidimetric inhibition immunoassay (Roche Diagnostics, Germany) on a Hitachi Modular P800i autoanalyzer (Manhaim, Germany). The reference range for healthy nondiabetic individuals is 4.8–5.9%. This method has an interassay coefficient of variation of 1.4%.

A 12-lead electrocardiogram was recorded in each patient just after hospital admission. Transthoracic echocardiography was performed by using a system V (Vingmed, GE, Horten, Norway) with a 2.5-MHz phased-array transducer. Recordings were taken on patients positioned in the left lateral decubitus position. The left ventricular ejection fraction was measured using a modified Simpson' s rule [6].

Coronary angiography, primary angioplasty, and stenting

All patients received chewable aspirin (300 mg, unless contraindicated) and clopidogrel (300 mg, loading dose) before coronary angiography. Angiographic data of the patients were obtained from the cardiac catheterization laboratory records. Emergency coronary angiography was performed by the percutaneous femoral approach. In all cases, nonionic low-osmolality contrast media was used. The contralateral artery was first injected. Infarct-related artery (IRA) was graded according to the Thrombolysis In Myocardial Infarction (TIMI) classification [7]. Heparin (10 000 U) was administered after coronary anatomy was defined. Coronary artery stenosis of more than 50% was considered clinically significant. Occlusion of the IRA was crossed by using a 0.014-inch guide wire. Primary coronary interventions including balloon angioplasty and/or stent implantation were performed only for IRA according to lesion anatomy. For each procedure, interventional success at the acute phase was defined as an obstruction and stenosis of the IRA having been reduced to less than 50% stenosis with TIMI 2 or 3 flows after primary PCI. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/h of intravenous heparin or 1 mg/kg/day of subcutaneous low-molecular weight heparin were given; aspirin (100 mg) and clopidogrel (75 mg) were continued in all patients. The use of tirofiban was left to the discretion of the operator.

Definitions

DM was considered to be present if patients had a history of diabetes that was controlled by diet, or with oral hypoglycemic agents or insulin, regardless of the duration, or were discharged from the hospital with a diagnosis of diabetes and/or hypoglycemic agents. Prediabetes was defined as HbA1c of 5.7–6.4% in patients without previously diagnosed DM. By using new ADA criteria [2], patients were classified into three groups: group I (HbA1c $\leq$ 5.6%); group II (HbA1c = 5.7–6.4%); and group III (HbA1c $\geq$ 6.5%).

The reperfusion time was defined as the time from symptom onset of chest pain to first balloon inflation. Door-to-balloon time was defined as the time between hospital admission and balloon inflation. Admission anemia was defined as a baseline hemoglobin concentration of less than 13 mg/dl in men and less than 12 mg/dl in women (World Health Organization definition). Cardiogenic shock was defined as marked and persistent (> 30 min) hypotension with systolic arterial pressure of less than 80 mmHg with signs of hypoperfusion due to left ventricular dysfunction, right ventricular infarction, and mechanical complications. Patients were also evaluated according to the Killip clinical examination classification [8]. Multivessel disease was defined by a stenosis of more than 50% in three major epicardial coronary arteries. Hypertension was defined as a history of hypertension for more than 1 year, which required the initiation of antihypertensive therapy by the primary physician. Positive family history for CAD was defined as documented evidence of CAD in a parent or sibling before 60 years of age. Acute stent thrombosis is defined as an abrupt onset of cardiac symptoms (i.e. an acute coronary syndrome) along with an elevation in levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 h, which is accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent. Reinfarction was described as

an elevation of serum creatine kinase-MB enzyme levels by two times of the upper limit of normal and ST-segment re-elevations. Major adverse cardiac events (MACE) were defined as cardiovascular mortality, reinfarction, and repeat target-vessel revascularization (percutaneous or surgical).

Follow-up

Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), stroke, cardiopulmonary resuscitation, transient pace intervention, intra-aortic balloon pump, atrial fibrillation, acute stent thrombosis, mortality, dialysis, cardiogenic shock, and MACE were recorded during the in-hospital period.

Statistical analysis

Quantitative variables were expressed as mean value ± standard deviation, and qualitative variables were expressed as percentage (%). The characteristics of the groups were compared by the use of analysis of variance for continuous variables and by the χ^2-statistic for categorical variables. Backward stepwise multivariate logistic regression analysis, which included variables with a *P* value of less than 0.1, was carried out to identify independent predictors of in-hospital mortality. Sex, age, DM, hypertension, anemia, multivessel disease, post-PCI TIMI grade 0/1, HbA1c, and admission creatinine of more than 1.5 mg/dl were entered into the model. A *P* value of less than 0.05 was considered statistically significant. All statistical studies were carried out with the SPSS program (version 15.0, SPSS, Chicago, Illinois, USA).

Results

Baseline characteristics

Patient characteristics in the study subgroups are summarized in Table 1. A total of 374 study patients (mean age: 55.9 ± 12.6 years, 318 men; mean HbA1c: 6.3 ± 1.3%) were divided into three groups: group I (HbA1c ≤ 5.6%, $n = 112$); group II (HbA1c 5.7–6.4%, $n = 180$); and group III (HbA1c ≥ 6.5%, $n = 82$). Group III were more likely to be female, older, and more commonly had hypertension, DM, Killip class of more than 1, earlier insulin usage, oral antidiabetic, angiotensin-converting enzyme/angiotensin receptor blocker use, and less smoker (Table 1). Sixty-six patients (17.6%) had a history of previously diagnosed DM. Diabetic patients had higher HbA1c levels (8.0 ± 1.7 vs. 5.9 ± 0.8%, $P < 0.001$) than nondiabetic patients. Fifty-one diabetic patients (77.3%) had HbA1c level of more than or equal to 6.5%. None of (0%) the diabetic patients had HbA1c in the normal range (HbA1c ≤ 5.6%). Twelve (18.2%) had unacceptably higher levels (≥ 10%). A total of 196 (63.6%) of the patients without a history of DM had elevated HbA1c level of more than or equal to 5.7%, with 31 (10.1%) of them having HbA1c level of more than or equal to 6.5% (Fig. 1), and these patients were not using any hypoglycemic agents. Prevalence of prediabetes was 44.1% ($n = 165$). The criteria of ADA (≥ 6.5%) had a sensitivity of 76% and specificity of 91% for the prediction of DM. The area under the receiver-operating characteristic curve with HbA1c used to detect DM was 0.91 (95% confidence interval: 0.87–0.95; Fig. 2).

Table 1 Baseline characteristics of study patients

	HbA1c groups			
	I (≤ 5.6) (n=112)	II (5.7–6.4) (n=180)	III (≥ 6.5) (n=82)	*P* value
Age (years)	51.2 (12.8)	56.3 (13)	60.5 (11.6)	<0.001
Male	105 (93.8)	155 (86.1)	58 (70.7)	<0.001
Anterior MI	51 (45.5)	86 (47.8)	35 (42.7)	0.74
Hypertension	30 (26.8)	84 (46.7)	46 (56.1)	<0.001
Diabetes mellitus	0 (0)	15 (8.3)	51 (62.2)	<0.001
Current smoker	87 (77.7)	118 (65.6)	47 (57.3)	0.009
Family history for CAD	53 (47.3)	76 (42.2)	37 (45.1)	0.69
Heart rate (beats/min)	76.3 (12)	77 (11.4)	79 (15.3)	0.31
SBP (mmHg)	125.5 (23.6)	125.8 (21.1)	127.9 (27.3)	0.75
Killip class >1	1 (0.9)	4 (2.2)	9 (11)	<0.001
By-pass	2 (1.8)	5 (2.8)	6 (7.3)	0.09
PCI	8 (7.1)	12 (6.7)	10 (12.2)	0.29
MI history	13 (11.6)	22 (12.2)	13 (15.9)	0.64
Reperfusion time (min)	223.2 (143.5)	228.3 (159.7)	257.3 (189.7)	0.3
Door-to-balloon time (min)	31 (23)	34 (21)	32 (20)	0.87
Earlier aspirin use	17 (15.2)	30 (16.7)	18 (21.9)	0.44
Earlier insulin use	0 (0)	0 (0)	15 (18.3)	<0.001
Earlier oral antidiabetic use	1 (0.9)	8 (4.4)	33 (40.2)	<0.001
Earlier β-blocker use	17 (15.2)	28 (15.6)	15 (18.3)	0.82
Earlier diuretic use	0 (0)	2 (1.1)	0 (0)	0.34
Earlier statin use	5 (4.5)	14 (7.8)	7 (8.5)	0.45
Earlier ACE/ARB use	18 (16.1)	43 (23.9)	34 (41.5)	<0.001

Mean values (standard deviation) and % (n) are reported for continuous and categorical variables, respectively.
ACE/ARB, angiotensin converting enzyme/angiotensin receptor blocker; CAD, coronary artery disease; HbA1c, hemoglobin A1c; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.

Laboratory findings

Table 2 lists the laboratory data of the patients. Bazal renal failure was more frequent in group III. Total and LDL cholesterol were lower in group III, but higher admission glucose, anemia, and body mass index were observed in group III (Table 2).

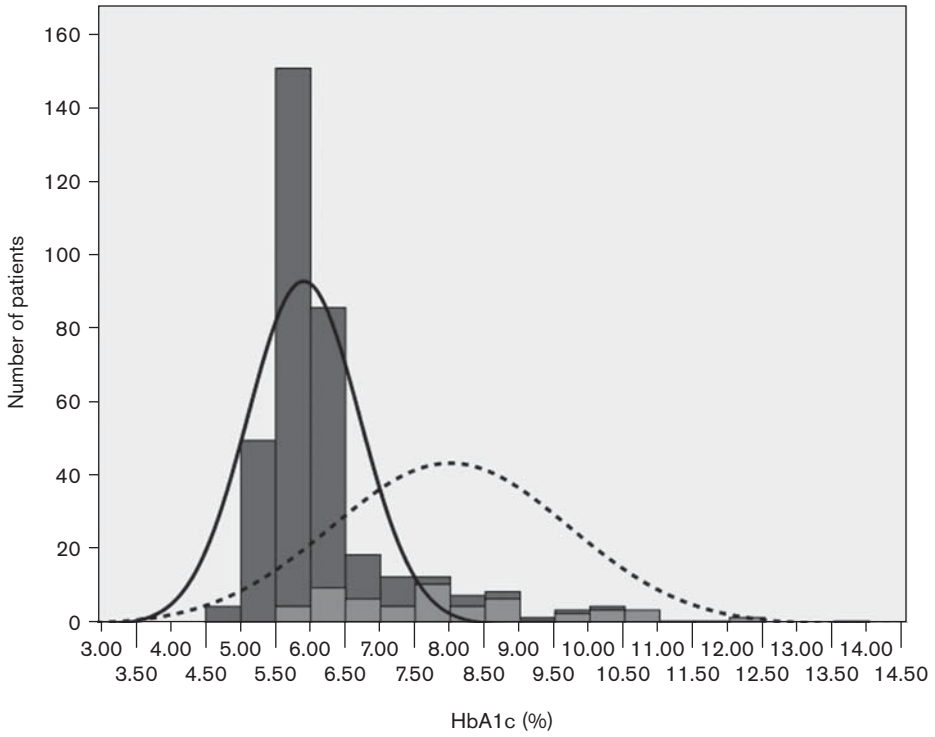
Angiographic and procedural characteristics

Angiographic and procedural characteristics are shown in Table 3. Mean left ventricular ejection fraction was less in group III. The other angiographic and procedural data were the same between the groups (Table 3).

In-hospital outcomes

Table 4 presents the in-hospital adverse outcomes after primary PCI. In-hospital mortality was higher in group III (11%) compared with group II (2.8%) and group I (0.9%; $P = 0.001$). Composite of death, reinfarction, and target-vessel revascularization (MACE) in the hospital were also higher in group III (12.2%) compared with other groups (group II, 5.6% vs. group I, 0.9%, $P = 0.003$; Fig. 3). There was a more complicated in-hospital outcome in

Fig. 1



Histogram showing the distribution of hemoglobin (Hb) A1c levels in patients with and without diabetes mellitus undergoing coronary artery bypass grafting. The gray histogram (patients with diabetes mellitus) and black histogram (patients without diabetes mellitus) show HbA1c distribution. Diabetic patients ($n=66$) had higher HbA1c levels (8.0 ± 1.7 vs. $5.9 \pm 0.8\%$, $P<0.001$) than nondiabetic patients ($n=308$).

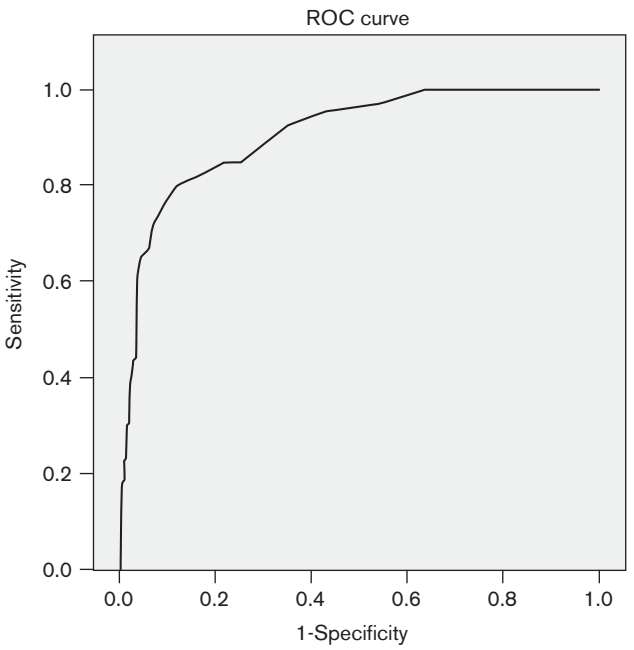
quartile III, with a higher incidence of cardiogenic shock and a higher percent of cardiopulmonary resuscitation (Table 4). Hospital stay was also longer in group III than others ($P = 0.007$). In-hospital mortality was similar between patients having HbA1c of more than or equal to 6.5% without previously diagnosed DM ($n = 4$, 12.9%) and with DM ($n = 5$, 9.8%, $P = 0.66$). After adjusting for baseline characteristics, HbA1c remained a strong independent predictor of in-hospital mortality (odds ratio: 1.412; 95% confidence interval: 1.031–1.935, $P = 0.03$; Table 5).

Discussion

The major findings of this single-center study, the first to date, examining the impact of HbA1c in patients undergoing primary PCI for STEMI, are that group III represents the highest risk population for in-hospital mortality and MACE with longer hospital stay. HbA1c was one of the independent predictors of in-hospital mortality. In addition, we found that more than half of the nondiabetic patients undergoing primary PCI had elevated HbA1c levels suggestive of prediabetes or DM.

The diagnosis of DM has been based on plasma glucose. After standardization of HbA1c assays, ADA recommended the use of the HbA1c test to diagnose DM and identify patients at higher risk for developing DM in

Fig. 2



The receiver-operating characteristic (ROC) curve for hemoglobin A1c for predicting diabetes mellitus. The area under the ROC curve = 0.91 (95% confidence interval: 0.87–0.95).

Table 2 Laboratory findings of patients

	HbA1c groups			
	I ($\leq$ 5.6) (n=112)	II (5.7–6.4) (n=180)	III ($\geq$ 6.5) (n=82)	P value
HbA1c (%)	5.4 (0.2)	6 (0.2)	8.2 (1.6)	<0.001
Admission creatinine (mg/dl)	0.87 (0.3)	0.86 (0.3)	0.96 (0.4)	0.06
Admission creatinine ($\geq$ 1.5 mg/dl)	4 (3.6)	4 (2.2)	6 (7.3)	0.14
Peak CK-MB (U/l)	185.6 (165.8)	160.7 (119.6)	191.2 (210.5)	0.24
Total cholesterol (mg/dl)	202.2 (50.6)	199.7 (47.5)	186.5 (39.8)	0.05
LDL cholesterol (mg/dl)	129.9 (39.5)	127.5 (39.1)	111.9 (33.3)	0.002
HDL cholesterol (mg/dl)	40.8 (11.6)	41.4 (10.2)	40.2 (10.4)	0.69
Triglycerides (mg/dl)	152.7 (89.8)	157.7 (91)	175.5 (106.5)	0.23
Admission glucose (mg/dl)	126.3 (27.6)	146.7 (43.2)	237 (101.7)	<0.001
Admission anemia	3 (2.7)	16 (8.9)	13 (15.9)	0.005
BMI (kg/m^2)	27.1 (3.6)	28 (4.2)	29.8 (5)	<0.001

Mean values (standard deviation) and % (n) are reported for continuous and categorical variables, respectively.
BMI, body mass index; CK-MB, creatinine kinase-MB; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

the future [2]. This test has lots of advantages to glucose including no need for fasting; less biologic variability, and preanalytic instability; unaffected by acute changes in glucose levels and higher standardization than glucose. In some genetic variants (e.g. HbS trait) and chemically modified derivatives, it can affect the accuracy of measurements. In these patients, assay selection method is very important. Acute blood loss and hemolytic anemia decreases the mean erythrocyte age and will falsely lower HbA1c results regardless of the assay method. In these patients, HbA1c should not be used to diagnose DM [9].

In a study by Kim *et al.* [10], they found that the optimal cut point of HbA1c for detecting undiagnosed DM was 6.1% (sensitivity 81.8%, specificity 84.9%). Hadjadj *et al.* [11] defined possible DM as those without previously diagnosed DM and HbA1c level of more than or equal to 6.5%. In the DETECT-2 trial [12], 19 000 patients were analyzed and showed that more than or equal to 6.5% level was optimal for detecting moderate retinopathy. There was no moderate retinopathy below this value. In another study, which was carried out in Malay ethnicity, the investigators concluded that more than or equal to 6.5% level was the cut point for detecting microvascular complications [13]. Therefore, in the last report of ADA, they decided to assign an HbA1c cut point of more than or equal to 6.5% for the diagnosis of DM [2], as long-term complications of DM, especially retinopathy, have good correlation with chronic glycemic levels. In this study, we used more than or equal to 6.5% for cut point like new ADA criteria, then the sensitivity was 76% and the specificity was 91%.

It is estimated that approximately 4% of patients admitted with STEMI are newly diagnosed DM [14]. But in this study, 10.1%, and in the study by Hadjadj *et al.* [11], 9.2% of patients had newly diagnosed DM by ADA criteria. In-hospital mortality was similar between patients having HbA1c level more than or equal to 6.5% without previously diagnosed DM and known DM in this study. In addition, HbA1c, even after adjustment on previously diagnosed DM, is a prognostic factor associated with mortality after STEMI. Therefore, HbA1c testing is very useful in the diagnosis of DM and prognosis.

Table 3 Angiographic and procedural characteristics of patients

	HbA1c groups			
	I ($\leq$ 5.6) (n=112)	II (5.7–6.4) (n=180)	III ($\geq$ 6.5) (n=82)	P value
Culprit lesion				0.8
LAD	53 (47.3)	88 (48.9)	36 (43.9)	
Circumflex	15 (13.4)	31 (17.2)	13 (15.9)	
RCA	44 (39.3)	60 (33.3)	33 (40.2)	
Others	0 (0)	1 (0.6)	0 (0)	
Number of diseased vessels				0.08
1	70 (62.5)	83 (46.1)	39 (47.6)	
2	24 (21.4)	56 (31.1)	27 (32.9)	
3	18 (16.1)	41 (22.8)	16 (19.5)	
Pre-TIMI grade				0.29
0/1	111 (99.1)	178 (98.9)	80 (97.6)	
2	0 (0)	2 (1.1)	2 (2.4)	
3	1 (0.9)	0 (0)	0 (0)	
Post-TIMI grade				0.25
0/1	1 (0.9)	4 (2.2)	5 (6.1)	
2	8 (7.1)	14 (7.8)	5 (6.1)	
3	103 (92)	162 (90)	72 (87.8)	
Stent	88 (78.6)	133 (73.9)	63 (76.8)	0.91
Stent length (mm)	18.8 (4.8)	18.2 (4.7)	17.5 (4.2)	0.22
Stent diameter (mm)	3.07 (0.33)	3.1 (0.36)	3.04 (0.37)	0.56
Stent type				0.22
BMS	88 (100)	128 (96.2)	63 (100)	
PES	0 (0)	3 (2.3)	0 (0)	
SES	0 (0)	2 (1.5)	0 (0)	
Proximal location of the lesion	83 (74.1)	120 (66.7)	57 (69.5)	0.41
LVEF (%)	46.4 (6.5)	44.9 (7.5)	42.5 (9.4)	0.003
Tirofiban	46 (41.1)	69 (38.3)	31 (37.8)	0.28
Success of procedure	108 (96.4)	166 (92.2)	75 (91.5)	0.28

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.
BMS, bare metal stent; HbA1c, hemoglobin A1c; LAD, left anterior descending; LVEF, left ventricular ejection fraction; PES, paclitaxel-eluting stent; RCA, right coronary artery; SES, sirolimus-eluting stent; TIMI, Thrombolysis in Myocardial Infarction.

ADA suggested to consider an HbA1c range of 5.7–6.4% for prediabetes as well, as HbA1c value of 5.7% was the best combination of sensitivity and specificity [15].

Table 4 In-hospital cardiac events and complications

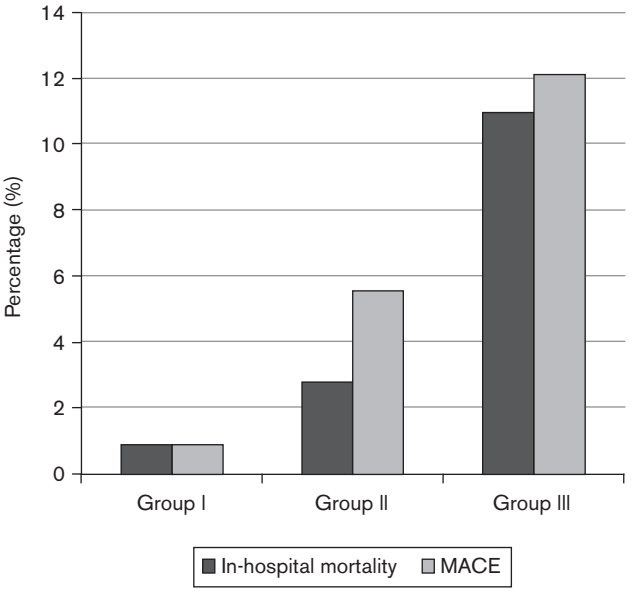
	HbA1c groups			
	I ($\leq$ 5.6) (n=112)	II (5.7–6.4) (n=180)	III ($\geq$ 6.5) (n=82)	P value
In-hospital mortality	1 (0.9)	5 (2.8)	9 (11)	0.001
Reinfarction	0 (0)	5 (2.8)	1 (1.2)	0.18
Target-vessel revascularization	0 (0)	3 (1.7)	0 (0)	0.2
MACE	1 (0.9)	10 (5.6)	10 (12.2)	0.003
Stroke	0 (0)	0 (0)	1 (1.2)	0.17
Serious ventricular arrhythmia	6 (5.4)	14 (7.8)	9 (11)	0.35
Cardiopulmonary resuscitation	1 (0.9)	5 (2.8)	10 (12.2)	<0.001
Cardiogenic shock	2 (1.8)	4 (2.2)	8 (9.8)	0.005
Intra-aortic balloon pump	0 (0)	3 (1.7)	3 (3.7)	0.13
Renal failure requiring dialysis	0 (0)	0 (0)	1 (1.2)	0.17
New atrial fibrillation	3 (2.7)	6 (3.3)	3 (3.7)	0.92
Complete atrioventricular block requiring transient pacemaker	3 (2.7)	8 (4.4)	2 (2.4)	0.61
Acute stent thrombosis	1 (0.9)	6 (3.3)	1 (1.2)	0.3
Time of hospital stay (days)	5.6 (2.4)	6.4 (3.2)	7.4 (5.9)	0.007

Mean values (standard deviation) and % (n) are reported for continuous and categorical variables, respectively.
MACE, major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization).

Prediabetes prevalence is also high with higher MACE ratio in this study. These patients should be informed of their increased risk of developing DM [15]. So effective strategies and regular screening for DM should be planned for this group.

Prospective studies have shown that higher HbA1c is associated with a risk of both STEMI and heart failure [16]. Corpus *et al.* [17] showed that an abnormal HbA1c level had prognostic significance in nondiabetic patients who underwent elective PCI. There are conflicting data about the prognostic value of HbA1c in acute STEMI. Hadjadj *et al.* [11] found that HbA1c values were not associated with post-STEMI prognosis in a small population. In 808 diabetic patients with acute STEMI, HbA1c did not predict mortality independently [18]. This study was retrospective, and more than two HbA1c values were measured within 2 years before admission. In another study by Timmer *et al.* [19], it was noted that HbA1c was not an independent predictor of increased mortality, but this study was carried out in STEMI, non-STEMI, and atypical chest pain. In the Optimal Therapy in Myocardial Infarction with the Angiotensin II Antagonist Losartan (OPTIMAAL) trial [20], in a large population, among patients with no history of DM, a 1% increase in the HbA1c level resulted in a 24% increase in mortality, but HbA1c level had no impact on mortality among diabetic patients. In the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction trial [21], HbA1c was an independent predictor of mortality in diabetic patients. There is a discrepancy between OPTIMAAL and Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction trial. HbA1c looses its predictive value in heart failure, and therefore, heart failure frequency is higher in the OPTIMAAL trial. This can explain the contrast between these two trials [22]. Chowdhury *et al.* [23] showed that elevated HbA1c was a risk marker for short-term mortality after STEMI in nondiabetic patients.

Fig. 3



Incidence of in-hospital mortality and major adverse cardiac events (MACE; cardiovascular death, reinfarction, and target-vessel revascularization) according to hemoglobin A1c groups.

Primary angioplasty is the best choice for treatment in acute STEMI, but above studies were made in heterogeneous groups. Therefore, this is the first study, to our knowledge, to explore the association of HbA1c with post-STEMI prognosis after primary PCI. HbA1c could be used as a simple prognostic and diagnostic test after primary PCI in coronary care unit, and it helps for strict control of complications and preventive strategies.

Study limitations

In this study, single-center data were used, which could result in selection bias. However, the patients were

Table 5 Multivariate predictors of in-hospital mortality

Variables	Wald	OR	95% CI	*P* value
Age	12.6	1.099	1.043–1.158	<0.001
HbA1c	4.6	1.412	1.031–1.935	0.03
Post-PCI TIMI grade 0/1	9.1	12.25	2.415–62.133	0.002

Sex, diabetes mellitus, hypertension, anemia, multivessel disease, and admission creatinine of more than 1.5 were also in the regression model.
CI, confidence interval; HbA1c, hemoglobin A1c; OR, odds ratio; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

admitted directly to our center to routinely undergo primary PCI for STEMI. We lacked detailed data on the duration of DM and microvascular complications. HbA1c can be affected in patients with hemoglobinopathies. But the assays that we used do not interfere with the abnormal hemoglobins. Hemolytic and iron-deficiency anemia also affect test results. But we could not evaluate these conditions. There is no long-term follow-up.

Clinical implications

Our findings suggest that in patients undergoing PCI for STEMI, HbA1c, irrespective of the presence or absence of DM, is associated with an increased in-hospital mortality and morbidity. The HbA1c test can also be used in the diagnosis of DM. The plasma HbA1c level could be a marker for risk stratification for STEMI patients, and new score models including HbA1c level should be investigated in future studies. Global cardio-metabolic risk control by intensive care should be a part of management in patients with high HbA1c.

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