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Prevalence of Glucose Abnormalities Among Patients Presenting with an Acute Myocardial Infarction

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Abstract

Background—Patients with an acute myocardial infarction (AMI) who have glucose abnormalities are at increased risk for death and adverse ischemic outcomes. The contemporary prevalence of glucose abnormalities among AMI patients in the U.S., as determined by HbA1c, is unknown.

Methods—Patients hospitalized with AMI in a 24-site U.S. AMI registry from 2005-2008 were examined for the presence of dysglycemia using HbA1c, which was analyzed at a core laboratory. Patients were categorized by American Diabetes Association guidelines as having diabetes (HbA1c $\geq 6.5\%$), pre-diabetes (HbA1c 5.7-6.4%), or normoglycemia. Baseline demographic, clinical, and metabolic characteristics, as well as long-term all-cause mortality, were compared among groups.

Results—Among 2853 patients with AMI, 1083 (38%) had diabetes, of which 196 (18%) were newly diagnosed. There were an additional 887 patients (31%) with pre-diabetes, and 883 patients (31%) who had normal glucose metabolism. Patients with metabolic abnormalities were older, more frequently female, and had higher prevalence of cardiac and non-cardiac comorbidities,

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including multivessel disease and left ventricular systolic dysfunction. Patients with increasing metabolic abnormalities had higher mortality over the 3-years after the AMI (8.6% in those with normoglycemia, 10.6% in pre-diabetes, 11.3% in newly diagnosed diabetes, and 20.3% in known diabetes; log rank $p < 0.001$).

Conclusions—In a large U.S. AMI registry, we found that nearly 7 in 10 patients had dysglycemia, with 38% having diabetes, and an additional 31% with pre-diabetes based on HbA1c levels. Over half of the patients who did not have a known diagnosis of diabetes at the time of admission had either newly diagnosed diabetes or pre-diabetes. Progressively greater severity of dysglycemia was also associated with incremental increase in long-term mortality. These data highlight the AMI hospitalization as a key opportunity to screen for glucose abnormalities, so that appropriate interventions and patient education efforts can be implemented prior to discharge.

Keywords

diabetes mellitus; myocardial infarction; HbA1c

Advances in invasive and medical management have significantly improved outcomes in all patients presenting with an acute myocardial infarction (AMI).¹ However, patients with diabetes (DM) continue to have a higher risk of recurrent adverse cardiac events after AMI, as well as higher short- and long-term mortality compared with patients without DM.²⁻³ Furthermore, patients with pre-DM are also at increased risk of these adverse events after AMI as compared with those having normal glucose values.⁴ While the prevalence of DM and pre-DM have been previously described in the AMI population, these data were based on oral glucose tolerance testing (which is rarely used in contemporary practice) and conducted over 10 years ago.⁵⁻⁶ Since that time, the profile of glucose abnormalities may have changed due to the rising prevalence of dysglycemia in the general population⁷ and the addition of HbA1c as a diagnostic criterion for DM and pre-DM.⁸ Accordingly, we sought to define the prevalence of dysglycemia among AMI patients enrolled in a multicenter U.S. registry from 2005-08, as assessed with HbA1c, in order to better understand the contemporary metabolic profiles of patients who present with AMI in the U.S. Finding high rates of DM and pre-DM would underscore the value of using an AMI hospitalization as an important opportunity to also address glucose metabolism and control.

METHODS

Study Population and Protocol

Details of the Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients' Health status (TRIUMPH) AMI registry have been previously published.⁹ Eligible patients had biomarker evidence of myocardial necrosis and additional clinical evidence supporting the diagnosis of an AMI. Baseline data were obtained through chart abstraction and a structured interview. Consenting patients had a fasting blood specimen collected prior to discharge, which was analyzed by a core laboratory (Clinical Reference Laboratory, Lenexa, KS). Known DM was defined as a chart-documented diagnosis of DM or glucose-lowering medications at the time of admission (except metformin or thiazolidinediones, as these may have been used for DM prevention [2

patients]). Congruent with the American Diabetes Association guidelines⁸, newly diagnosed DM was defined as HbA1c \geq 6.5%, pre-DM was defined as HbA1c 5.7-6.4%, and normal glucose metabolism was defined as HbA1c $<$ 5.7%. Mortality at 3-years post-AMI was assessed through a combination of follow-up interviews and a query of the Social Security Death Masterfile. Each participating hospital obtained Institutional Research Board approval, and all patients provided written informed consent.

Statistical Analysis

Baseline characteristics and in-hospital treatments of patients with the 4 different levels of glucose metabolism (known DM, newly diagnosed DM, pre-DM, normoglycemia) were compared using ANOVA for continuous variables and chi-square tests for categorical variables. In addition, patients with known DM were compared with those with newly diagnosed DM using *t*-tests for continuous variables and chi-square tests for categorical variables. Finally, we compared 3-year mortality rates across the 4 groups using Kaplan-Meier curves. All analyses were conducted using SAS v9.2 (SAS Institute, Inc., Cary, NC), and statistical significance was determined by a 2-sided *p*-value of $<$ 0.05. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

RESULTS

Patient Population

Among 4340 patients enrolled in TRIUMPH, 2853 (66%) consented to and provided blood samples that were analyzed for HbA1c. Patients who participated in the laboratory sub-study (vs. not) were more likely to be younger, male, white, current smokers, and have depressive symptoms, although the prevalence of known DM and chart-documented HbA1c, fasting glucose, and cholesterol levels were similar (Supplemental Table 1). Among the 2853 patients with AMI who participated in the laboratory sub-study, 1083 (38%) had DM, of which 196 (18%) had not been previously diagnosed as having DM. There were an additional 887 patients (31%) who had pre-DM, which left only 883 patients (31%) with normal glucose metabolism. Among the 1966 patients in TRIUMPH who did not have DM at the time of admission of their AMI, 10% had new DM (i.e., previously undiagnosed) and 45% had pre-DM.

Comparisons Across Metabolic Groups

There were multiple demographic and clinical differences among the 4 metabolic groups (Table 1). Patients with metabolic abnormalities were older, more frequently female, non-white race, and had greater prevalence of cardiac and non-cardiac comorbidities. Patients with DM and pre-DM were less likely to present with ST-elevations (vs. non-ST-elevation AMI) but were more likely to have multivessel disease and left ventricular systolic dysfunction. In addition, patients with increasing metabolic abnormalities had higher HbA1c levels, higher fasting glucose levels, higher insulin levels, and higher triglyceride levels (Table 2).

Compared with known DM, newly-diagnosed DM patients were more likely to be current smokers (new vs. known: 43% vs. 33%, $p<0.001$), had fewer non-cardiac comorbidities, and lower proportion of those with a history of prior coronary disease (Table 1). Patients with newly diagnosed DM were less likely to have multivessel disease (50% vs. 61%, $p=0.006$) and more likely to present with an ST-elevation AMI (41% vs. 32%, $p=0.013$). Patients with newly-diagnosed DM, on average, had milder glucose abnormalities compared with known DM, with lower mean HbA1c levels (7.6 vs. 8.1%, $p=0.002$) and fasting glucose levels (123 vs. 145 mg/dL, $p=0.001$), although fasting insulin levels were similar (21.1 vs. 21.4, $p=0.912$; Table 2).

Regarding long-term outcomes, patients with increasing metabolic abnormalities had increasing risk of mortality over the 3-years after the AMI. The Kaplan-Meier estimated rates of death at 3 years after AMI were 8.6% among those with normoglycemia, 10.6% in those with pre-DM, 11.3% in those with newly diagnosed DM, and 20.3% among those with known DM (log rank $p<0.001$; Figure 1).

DISCUSSION

In a large, contemporary, multicenter U.S. registry, we found that nearly 70% of patients who present with an AMI have abnormal glucose metabolism. Nearly 2 out of every 5 patients with an AMI have overt DM, with 18% of these patients without an established DM diagnosis. Furthermore, an additional 31% of patients with AMI have pre-DM. Over half of patients without a known diagnosis of DM at admission for AMI had either DM or pre-DM. These results highlight the epidemic of glucose abnormalities in the US and the very high prevalence of dysglycemia in patients with coronary artery disease—a trend that is likely to be accelerated in the future.⁷ In addition, increasing dysglycemia was associated with incremental increased risk of long-term mortality. Our findings suggest that the AMI hospitalization may be a key opportunity to screen for glucose abnormalities, which may strengthen secondary prevention efforts (including medical and lifestyle interventions) in this high-risk patient population.

Prior studies have found varying levels of abnormal glucose metabolism among patients with coronary artery disease. Among European patients, the prevalence of DM ranges from 20-30% (with higher prevalence in AMI patients⁵) and ~35% having pre-DM.⁶ In the China Heart Study, the prevalence of abnormal glucose metabolism was even higher, with DM estimated in ~53% and pre-DM in 24%.¹⁰ However, each of these studies focused on screening via oral glucose tolerance testing. Previously recommended by the European Society of Cardiology, this was not included as the primary method of screening in the most recent guideline statement¹¹ due to the inconvenience of the multi-step testing and the emergence of HbA1c as the primary standard of screening, diagnosis, and management of patients with DM. Oral glucose tolerance testing is likely more sensitive than HbA1c for identifying glucose abnormalities¹²⁻¹⁴; however, there remains some controversy regarding its accuracy in the acute setting of the myocardial infarction.¹⁵ In contrast, although there are well known limitations to the use of HbA1c (e.g., blood transfusions, hemoglobinopathies, prolonged stress hyperglycemia, etc.), the representation of chronic glycemic control makes it particularly attractive in the setting of the acute adrenergic surge

of an AMI. Given the widespread use of HbA1c in the diagnosis and management of patients with DM, we believe that the use of HbA1c is a key strength of our study.

There are potential limitations to our study that merit further discussion. First, although TRIUMPH included 24 rural, suburban, and urban hospitals across the U.S. and the patients represented a broad range of socioeconomic and demographic characteristics, it is uncertain if our findings are representative of the U.S. AMI population. However, we are unaware of any large studies examining the prevalence of glucose abnormalities in U.S. patients presenting with an AMI, which provides important epidemiologic insight into the prevalence of this risk factor. Second, not all TRIUMPH patients participated in the laboratory sub-study. While there were demographic and clinical differences between those who did and those who did not participate, the frequency of known DM did not differ between groups nor did any of the metabolic factors that were available by chart abstraction, supporting the generalizability of our findings.

In conclusion, in a large, contemporary, U.S. population of AMI patients, we found that nearly 7 in 10 patients had dysglycemia, with 38% having diabetes, and an additional 31% with pre-diabetes based on HbA1c levels. Over half of the patients who did not have a known diagnosis of diabetes at the time of admission had either a new diagnosis of diabetes or pre-diabetes—emphasizing the importance of screening AMI patients with a HbA1c to detect these potentially modifiable risk factors. In addition, progressively greater severity of dysglycemia was associated with incremental increase in long-term mortality. These data improve our understanding of the extremely high prevalence of dysglycemia among patients who present with an AMI and suggest that the AMI hospitalization is an important opportunity to screen for dysglycemia, which could improve secondary prevention efforts in these high-risk patients.

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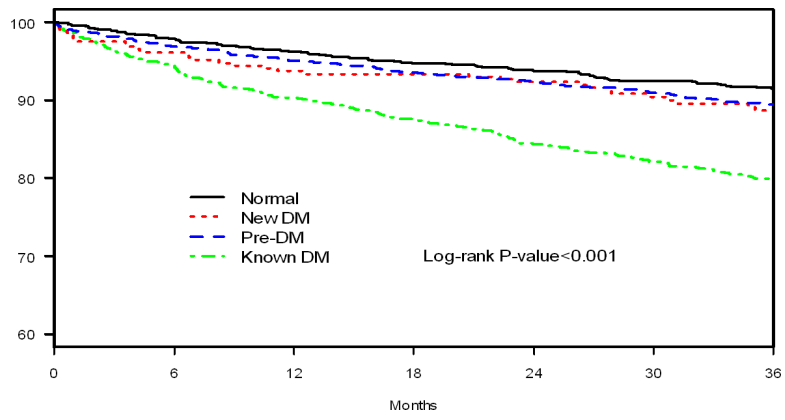


Figure 1.
Kaplan Meier survival curves by degree of glucose dysmetabolism

Table 1
Demographic and clinical characteristics of AMI patients according to degree of glucose dysmetabolism

	Known DM n=887	New DM n=196	Pre-DM n=887	Normal n=883
Age (years)	60.0 ± 11.5	58.6 ± 10.7	59.5 ± 12.8	55.9 ± 12.4
Male	62.7%	64.8%	67.4%	75.5%
White race	59.8%*	51.8%*	71.2%	78.2%
Currently working	35.9% [‡]	53.8% [‡]	51.0%	60.5%
Current smoking	32.7%*	42.5%*	45.8%	44.3%
Prior AMI	26.8% [‡]	16.8% [‡]	19.3%	15.9%
Prior angioplasty	25.6% [‡]	12.8% [‡]	19.4%	15.5%
Prior bypass graft surgery	17.9% [‡]	10.2% [‡]	9.5%	6.9%
Peripheral vascular disease	6.4%	5.1%	3.7%	2.7%
Prior stroke	7.1% [‡]	4.1% [‡]	3.4%	3.9%
Prior heart failure	15.8%*	10.2%*	5.4%	4.0%
Estimated GFR (mL/min/1.73 m ²)	70.7 ± 31.1 [‡]	82.7 ± 26.3 [‡]	77.2 ± 24.3	81.4 ± 24.1
Depression	26.7% [‡]	13.0% [‡]	16.9%	19.9%
ST-elevation AMI	31.6%*	40.8%*	47.8%	50.8%
Peak troponin (ng/dL)	21.6 ± 62.5	29.4 ± 106.4	30.7 ± 72.1	34.5 ± 79.1
Multivessel disease	61.1% [‡]	50.0% [‡]	46.3%	40.9%
Left ventricular systolic dysfunction	21.9%	20.4%	16.1%	17.8%
GRACE mortality risk score	106.5 ± 29.8 [‡]	99.0 ± 26.8 [‡]	99.3 ± 29.6	91.8 ± 29.0

All comparisons across the 4 groups are significantly different among groups at p<0.001 except LV systolic dysfunction (p=0.016) Pairwise comparisons of Known DM vs. New DM

* p<0.05

[‡] p<0.01

[‡] p<0.001

Table 2

Metabolic characteristics of AMI patients according to degree of glucose dysmetabolism

	Known DM n=887	New DM n=196	Pre-DM n=887	Normal n=883
Hemoglobin A 1c (%)	8.1 ± 2.1 [†]	7.6 ± 1.7 [†]	6.0 ± 0.2	5.3 ± 0.3
Fasting glucose (mg/dL)	179.7 ± 82.6 [‡]	146.2 ± 51.9 [†]	114.7 ± 27.4	108.5 ± 22.5
Insulin level (µIU/mL)	21.4 ± 37.3	21.1 ± 24.0	17.7 ± 26.4	15.3 ± 22.1
Diabetes medications on arrival	69.8% [‡]	0.0% [‡]	0.2%	0.0%
Diabetes medications at discharge	83.4% [‡]	25.6% [‡]	2.3%	0.8%
Body mass index (kg/m2)	31.9 ± 7.4 [*]	30.7 ± 5.9 [*]	29.1 ± 5.9	27.9 ± 5.6
History of hypertension	83.9% [‡]	62.2% [‡]	65.2%	49.4%
Systolic blood pressure (mmHg)	145.7 ± 30.4	146.5 ± 27.3	140.7 ± 29.8	140.3 ± 29.8
Diastolic blood pressure (mmHg)	83.2 ± 19.5 [†]	86.8 ± 17.6 [†]	82.2 ± 18.6	82.7 ± 18.7
History of dyslipidemia	62.2% [‡]	41.8% [‡]	46.4%	38.1%
Total cholesterol (mg/dL)	152.1 ± 42.6 [†]	162.0 ± 36.8 [†]	159.9 ± 36.2	153.9 ± 35.6
Fasting triglycerides (mg/dL)	168.8 ± 130.8	170.3 ± 115.2	150.1 ± 99.6	140.6 ± 81.2
Fasting HDL-C (mg/dL)	38.7 ± 10.1	39.7 ± 9.9	40.9 ± 11.1	40.1 ± 10.7
LDL-C (mg/dL)	92.0 ± 35.2 [†]	100.6 ± 29.8 [†]	98.4 ± 30.8	93.9 ± 30.2

All comparisons across the 4 groups are significantly different among groups at p<0.001 except diastolic blood pressure (p=0.02) Pairwise comparisons of Known DM vs. New DM

* p<0.05

[†] p<0.01

[‡] p<0.001