Recognition of Incident Diabetes Mellitus During an Acute Myocardial Infarction

Suzanne V. Arnold, MD, MHA; Joshua M. Stolker, MD; Kasia J. Lipska, MD, MHS; Philip G. Jones, MS; John A. Spertus, MD, MPH; Darren K. McGuire, MD, MHS; Silvio E. Inzucchi, MD; Abhinav Goyal, MD, MHS; Thomas M. Maddox, MD, MSc; Marcus Lind, MD; Divya Gumber, MD; Supriya Shore, MD; Mikhail Kosiborod, MD

Background—Diabetes mellitus (DM) is common in patients hospitalized with an acute myocardial infarction (AMI), representing in some cases the first opportunity to recognize and treat DM. We report the incidence of new DM and its recognition among patients with AMI.

Methods and Results—Patients in a 24-site US AMI registry (2005–08) had glycosylated hemoglobin assessed at a core laboratory, with results blinded to clinicians and local clinical measurements left to the discretion of the treating providers. Among 2854 AMI patients without known DM on admission, 287 patients (10%) met criteria for previously unknown DM, defined by a core laboratory glycosylated hemoglobin of ≥6.5%. Among these, 186 (65%) were unrecognized by treating clinicians, receiving neither DM education, glucose-lowering medications at discharge, nor documentation of DM in the chart (median glycosylated hemoglobin of unrecognized patients, 6.7%; range, 6.5–12.3%). Six months after discharge, only 5% of those not recognized as having DM during hospitalization had been initiated on glucose-lowering medications versus 66% of those recognized (P<0.001).

Conclusions—Underlying DM that has not been previously diagnosed is common among AMI patients, affecting 1 in 10 patients, yet is recognized by the care team only one third of the time. Given its frequency and therapeutic implications, including but extending beyond the initiation of glucose-lowering treatment, consideration should be given to screening all AMI patients for DM during hospitalization. Inexpensive, ubiquitous, and endorsed as an acceptable screen for DM, glycosylated hemoglobin testing should be considered for this purpose. (Circ Cardiovasc Qual Outcomes. 2015;8:260-267. DOI: 10.1161/CIRCOUTCOMES.114.001452.)

Key Words: diabetes mellitus ■ hemoglobin A, glycosylated ■ myocardial infarction ■ quality of health care

Approximately one third of patients hospitalized for an acute myocardial infarction (AMI) have pre-existing diabetes mellitus (DM).1,2 Despite its high prevalence in the AMI population, the diagnosis of DM has traditionally been deferred to the outpatient setting. This is mostly because of the well-known dysregulation of glucose metabolism during an AMI,3 making hyperglycemia common and confounding the accuracy of diagnosing DM using plasma glucose levels alone.3,4 However, the AMI hospitalization is frequently the first opportunity to identify and treat previously unrecognized DM, particularly for those patients with little or no routine healthcare before their AMI event. As a result, identifying the presence of underlying DM during the AMI may represent a unique opportunity for better recognition and earlier treatment of DM,5,6 with implications for chronic DM management—including DM education, as well as initiation and titration of antihyperglycemic therapy—and informing the care of coronary disease—including revascularization options, antiplatelet therapy, and choice of antihypertensive medications.

Previous studies using oral glucose tolerance testing—a highly sensitive method for detecting metabolic abnormalities—have estimated that in 1 in 4 patients with coronary artery disease but without previously established DM have undiagnosed DM.7–9 In 2010, the American Diabetes Association adopted glycosylated hemoglobin (HbA1c) as a reliable measure of chronic glycemia to help diagnose DM, independent from serum glucose levels,10 and this has been generally suggested in AMI patients with hyperglycemia but without history of DM to identify patients who may benefit from the initiation of lifestyle counseling or pharmacological glucose-lowering therapy.11 Importantly, however, screening for underlying DM is not mentioned in the most recent US AMI guidelines.12
WHAT IS KNOWN

- In patients hospitalized with an acute myocardial infarction, concomitant diabetes mellitus is common, and sometimes it is not yet diagnosed before the hospitalization.
- Identifying diabetes mellitus during the acute hospitalization would allow for earlier treatment of diabetes mellitus (through education and possibly medication) and could have important implications for the acute care of coronary disease (including revascularization options, antiplatelet therapy, and choice of antihypertensive medications).

WHAT THE STUDY ADDS

- Among 2854 patients from 24 US hospitals without known diabetes mellitus on admission who were admitted with an acute myocardial infarction, 10% met criteria for previously unknown diabetes mellitus (core laboratory glycosylated hemoglobin ≥26.5%). Only one third of these patients were recognized by the treating clinicians during the hospitalization as having diabetes mellitus, and patients who were unrecognized during the acute hospitalization were rarely recognized 6 months after.
- Given the frequency of underlying diabetes mellitus in this population and the importance of identifying the diagnosis acutely—both for glycemic control and treatment of the presenting coronary syndrome—these results support the universal screening of patients with an acute myocardial infarction for diabetes mellitus.

To understand both the prevalence of underlying DM that was previously undiagnosed and its frequency of recognition among patients hospitalized with AMI, we systematically screened for DM in a large, multicenter AMI registry using core laboratory measurement of HbA1c. In this context, we evaluated how commonly those meeting diagnostic HbA1c criteria for DM were recognized by their local care providers.

Methods

Study Population and Protocol
Between June 2005 and December 2008, 4340 patients from 24 US hospitals were enrolled into the Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients’ Health Status (TRIUMPH) study of patients with AMI. Patients were required to have biomarker evidence of myocardial necrosis and additional clinical evidence supporting the diagnosis of an AMI, including prolonged ischemic signs/symptoms (≥20 minutes) or electrocardiographic ST-segment changes during the initial 24 hours of admission. Baseline data were obtained through chart abstraction and a structured interview by trained research staff within 24 to 72 hours after admission. All enrolled patients were asked to participate in the laboratory substudy, and consenting patients had fasting blood samples drawn before discharge, which were processed, refrigerated, and sent by overnight mail to the TRIUMPH core laboratory (Clinical Reference Laboratory, Lenexa, KS) on a daily basis. These core laboratory samples were analyzed for glucose and HbA1c, among other markers, with test results blinded to treating providers. HbA1c was assessed with the Bio-Rad VARIANT II assay, which is certified by the National Glycohemoglobin Standardization Program and standardized to the Diabetes Control and Complications Trial reference assay. Laboratory values drawn for clinical reasons were recorded from the hospital chart, including up to 3 values of fasting plasma glucose, random plasma glucose on admission, and HbA1c values that were obtained as a part of routine clinical care.

Detailed follow-up was attempted on all survivors at 1, 6, and 12 months after AMI. Patients within TRIUMPH could opt for follow-up 6 months after AMI by telephone (interview-only) or an in-home visit, which allowed for the collection of laboratory data. Medications were recorded at admission, discharge, and each follow-up time point. Each participating hospital obtained Institutional Research Board approval, and all patients provided written informed consent for baseline and follow-up assessments.

DM Diagnosis and Recognition

Known DM was defined as a chart-documented diagnosis of DM or treatment with glucose-lowering medications at the time of admission. Underlying DM that was previously undiagnosed was defined as the absence of known DM and a core laboratory HbA1c of ≥6.5% (data blinded to clinicians) or, if the patient did not consent to the laboratory substudy, by a chart HbA1c of ≥6.5%. If both core and chart HbA1c levels were unavailable, DM could additionally be diagnosed if the patient had (1) ≥2 fasting plasma glucose levels of ≥200 mg/dL or (2) fasting plasma glucose of ≥200 mg/dL and random plasma glucose (at presentation) of ≥200 mg/dL. Patients with previously undiagnosed DM were considered recognized if they received DM education (which was systematically queried on the study case report form) during the AMI hospitalization, were discharged on any glucose-lowering medication, or had a primary or secondary discharge diagnosis code of 250.xx; otherwise, they were considered unrecognized.

We also performed 2 sensitivity analyses. First, as we defined DM by core laboratory HbA1c, some patients could have had HbA1c levels drawn clinically that were <6.5% and may have been appropriately not recognized as having DM. As such, we excluded patients who had a chart HbA1c of <6.5% who did not have other supporting diagnostic evidence of DM (ie, ≥2 fasting plasma glucose levels of ≥200 mg/dL or fasting plasma glucose of ≥200 mg/dL and random plasma glucose ≥200 mg/dL). Second, we examined the frequency of recognition among only those patients who had a core HbA1c level available (as this was a reasonably random sample of the TRIUMPH patients), to assure that no bias was introduced by including patients with missing core HbA1c results.

Statistical Analysis

Among patients without known DM, we first compared baseline characteristics between those who were and were not screened for DM with an HbA1c test using t-tests for continuous variables and χ² test for categorical variables. We then explored the variability of HbA1c testing among the hospitals in TRIUMPH by constructing a hierarchical logistic regression model with site included as a random effect. Patient factors that were hypothesized to be associated with assessment of HbA1c during AMI were included in the model for patient-level adjustment and included the following: age, sex, race, high school or greater education, current smoking status, ST-segment-elevation AMI, body mass index, history of hypertension, serum creatinine, fasting plasma glucose, and admission plasma glucose. Predictor variables were mean-centered within hospital, to adjust for the differences between sites, and site-level variation was explored with a median odds ratio, which estimates the average relative difference in odds ratios of 2 hypothetical patients being screened for DM with an HbA1c if enrolled at 2 different sites. Smoothed rates of HbA1c checking at the hospitals in TRIUMPH were also reported.

Next, we compared baseline characteristics among patients with known DM, those with underlying DM that was previously undiagnosed—recognized and unrecognized—and those with no DM using...
1-way ANOVA for continuous variables and χ² test for categorical variables. We also compared baseline characteristics between those with underlying DM that was recognized versus unrecognized using t-tests for continuous variables and χ² test for categorical variables. We compared the chart data available to clinicians, including frequency of HbA1c blood tests, between groups. Finally, we used χ² tests to compare the frequency of glucose-lowering medication prescription (oral medication or insulin) at 6 months after AMI between those with initially recognized versus unrecognized DM during the AMI hospitalization, stratified by HbA1c category at baseline (6.5%–6.9%; 7.0%–7.9%; ≥8%).

For the multivariable model that evaluated variability in HbA1c testing across the hospitals, predictor data were missing in 14% of patients (only 2% were missing data on >1 variable; the highest missing rate for any one variable was 10%). Missing data were imputed using multiple imputation methods. The imputation model included the dependent and all independent variables, as well as the study site. Iterative sequential regression was used to sampling missing values from the predictive distribution of each variable conditional on all other variables. Fifty randomly imputed data sets were generated in this way; analyses were replicated on each imputed data set and the model estimates were pooled across imputations. All analyses were conducted using SAS version 9.2 (SAS Institute, Inc, Cary, NC) and IVWare (Imputation and Variance Estimation Software; University of Michigan’s Survey Research Center, Institute for Social Research, Ann Arbor, MI), and statistical significance was determined by a 2-sided P value of <0.05.

Results

Patient Population

Of 4340 patients enrolled in TRIUMPH, 1339 patients had prevalent DM (ie, known before admission). Of the remaining 3001 patients without prevalent DM, 1196 patients (39.9%) were screened for DM locally with an HbA1c, of whom 154 (12.9%) had underlying DM. Of these, 57.1% were recognized as having DM. Of the 1805 patients who did not have an HbA1c checked locally, metabolic data were available for 1658, of whom 133 (8.0%) had underlying DM—9.8% of whom were recognized as having DM. Overall, among 2854 patients without prevalent DM who had metabolic data available, 287 patients (10.1%) were identified through core laboratory assessment (data blinded to clinicians) as having underlying but previously undiagnosed DM. Of these, 101 patients (35%) were recognized by the treating physicians as having DM, evidenced by provision of DM education for 68 patients (67%), prescription of glucose-lowering medication at discharge for 69 patients (68%; 48% received both interventions), and diagnosis code documentation alone in 12 patients (12%). In total, of the 4193 patients with metabolic data, 31.9% had prevalent DM and 6.8% had underlying DM that had not been previously diagnosed—2.4% of patients with AMI were recognized as having newly diagnosed DM and 4.4% of patients with AMI had underlying DM that remained persistently undiagnosed.

Screening for DM

The baseline characteristics of patients without prevalent DM who were and were not screened with an HbA1c locally are shown in Table 1. Patients who were white, presented with an ST-segment–elevation AMI, had multivessel coronary artery disease, and those with higher glucose levels were more likely to be screened with an HbA1c during the AMI hospitalization. However, there was substantial variability across sites in terms of screening rates, with a smoothed range of 8% to 82% of patients without known DM being screened with an HbA1c (Figure). Furthermore, after adjusting for patient factors, there remained large site-level variability in HbA1c checking, with a median odds ratio of 4.56 (95% confidence interval, 3.11–8.41), indicating that 2 hypothetically identical patients would have an over 4-fold greater likelihood of being screened with an HbA1c at 1 random hospital when compared with another.

DM Recognition

The baseline characteristics of patients with underlying DM that had not been previously diagnosed, along with the characteristics of those with known DM and those with no DM, are shown in Table 2. Patients whose DM was recognized were younger, more likely to be white, and were less likely to have a history of coronary artery disease. Fasting plasma glucose levels were higher among recognized versus unrecognized patients (175 versus 135 mg/dL; P<0.001) as were HbA1c levels (8.6% versus 6.9%; P<0.001). Although all measures of glycemic control were worse among those with recognized DM, the unrecognized patients still exhibited a wide range of glycemic control (HbA1c, 6.5%–12.3%), with a sizable proportion (20%) having an HbA1c of ≥7% (a generally accepted threshold for pharmacological treatment).

Recognized patients were more likely than unrecognized patients to have chart data available that supported the diagnosis of DM (Table 3). HbA1c was far more likely to be checked clinically in recognized versus unrecognized patients (87.1% versus 35.5%; P<0.001). In addition, more recognized patients had fasting and random plasma glucose levels that exceeded traditional thresholds for the outpatient diagnosis of DM. However, 60.8% of patients whose DM was not recognized still had at least 1 diagnostic criterion for DM present and 35.5% had ≥2 diagnostic criteria available to local clinicians in the chart.

Follow-Up Glucose-Lowering Treatment

At hospital discharge, 68.3% of recognized patients were prescribed at least 1 glucose-lowering medication at discharge. The majority of recognized patients (66.2%) were still on glucose-lowering medications at 6 months: 31.6% of those with HbA1c 6.5 to 6.9% during the AMI hospitalization, 66.7% of those with HbA1c 7% to 7.9%, and 85.7% of those with HbA1c ≥8%. By definition, no unrecognized patients were discharged on glucose-lowering medication. At 6 months, only 4.8% of unrecognized patients had been initiated on any such medication (P<0.001): 2.4% of those with HbA1c 6.5 to 6.9%, 20.0% of those with HbA1c 7% to 7.9%, and 20.0% of those with HbA1c ≥8%.

Sensitivity Analyses

There were 14 patients who had DM, as evidenced by a core laboratory HbA1c of ≥6.5%, who had a chart HbA1c of <6.5% and did not have other diagnostic evidence of DM. After excluding these 14 patients, the frequency of recognition was 37%, compared with 35% in the primary analysis. In the second sensitivity analysis, we excluded 888 patients who did not have a core HbA1c level available. Of the remaining 1966 patients, 196 patients (10.0%) were newly diagnosed as
Race

Male, sex 71.1% 70.0% 0.540
Age, y 58.1±12.4 58.5±12.6 0.299
Married 57.5% 52.4% 0.006
Body mass index, kg/m² 28.8±5.9 28.5±5.9 0.139
High school education or greater 82.0% 81.2% 0.567
Chronic lung disease 4.2% 8.3% <0.001
Previous bypass graft surgery 7.4% 9.0% 0.105
Previous angioplasty 15.4% 18.1% 0.055
Previous myocardial infarction 15.2% 19.6% 0.002
Hypertension 58.1% 59.3% 0.504
Dyslipidemia 40.5% 45.7% 0.005
Current smoker 46.3% 41.9% 0.017

IQR, interquartile range; and LV, left ventricular.

Depression 14.9% 17.2% 0.118
Fasting glucose, mg/dL 117.9±33.3 114.4±28.2 0.003
Random glucose, mg/dL 140.8±55.1 123.6±35.5 <0.001
LV systolic dysfunction 54.8% 43.8% <0.001
St-segment–elevation myocardial infarction
Peak troponin, median (IQR), ng/dL 7.6 (1.9–31.3) 5.6 (1.5–26.4) <0.001
Multivessel disease, ≥2 vessels 70.2% 40.9% <0.001
Random glucose, mg/dL 140.8±55.1 123.6±35.5 <0.001
Fasting glucose, mg/dL 117.9±33.3 114.4±28.2 0.003
Underlying diabetes mellitus 19.6% 8.3% <0.001
Recognized 7.4% 0.8%<0.001
Unrecognized 5.5% 7.2%

HbA1c indicates glycosylated hemoglobin; GFR, glomerular filtration rate; IQR, interquartile range; and LV, left ventricular.

Table 1. Baseline Characteristics of Patients Without Known Diabetes Mellitus Who Were Versus Were Not Screened for Diabetes Mellitus With an HbA1c

During hospitalization, indicating that they were also unlikely to be subsequently recognized as outpatients.

Although screening AMI patients with an HbA1c locally did not always result in physician recognition of the underlying DM, there was, as expected, a strong association between the 2. These data highlight a continued need to screen AMI patients with HbA1c to improve the rate of DM recognition during the hospitalization; this would not only guide initiation of glucose management interventions (when needed) but also inform several key aspects of post-MI cardiovascular care. It is important to note that although European guidelines recommend screening all patients with AMI for DM, there is no such discussion in the US AMI guidelines. Interestingly, however, the guidelines do include several treatment recommendations that rely on the knowledge of the presence of DM, such as timing and type of revascularization and addition of angiotensin-converting enzyme inhibitors or aldosterone inhibitors. Although some patient factors, such as body weight and glucose levels, were associated with increased screening and recognition of DM, even after adjusting for these factors, there was substantial site-level variability, indicating that site-level practices (eg, including HbA1c testing in preprinted AMI order sets) likely play an important role in screening for DM. A scientific statement from the American Heart Association recommended screening patients with AMI that have evidence of hyperglycemia with an HbA1c. Although this would effectively identify most AMI patients with high HbA1c levels, it would still miss ≈30% of patients with DM and would also potentially delay the diagnosis of DM, which could affect acute treatment decisions (ie, choice of bypass surgery or multivessel stenting). Removing DM screening from the thought processes of clinicians—who tend to focus on the AMI care alone instead of management of chronic diseases—and incorporating universal HbA1c screening into standardized AMI care would likely be most effective in increasing screening rates. Incorporation of screening recommendations for DM in the US AMI guideline statements would also likely improve recognition of underlying DM, with possible effect on both in-hospital and postdischarge management of these patients.

Discussion

In a large, contemporary multicenter US registry, we found that 10% of patients with AMI and no previous DM diagnosis have underlying DM, defined as an HbA1c of ≥6.5%. Only one third of these patients were actually recognized during the hospitalization as having DM. Not surprisingly, patients whose DM was not recognized by clinicians generally had milder forms of DM compared with DM that was recognized, with lower HbA1c and glucose levels. However, 20% of patients with DM that was not recognized during AMI hospitalization had core HbA1c values of ≥7%, with a range up to 12.3%. Importantly, initiation of glucose-lowering medications during the 6 months after discharge was uncommon among patients who were not recognized as having DM having DM. Among these, 70 patients (36%) were recognized as having DM.
Clinical Implications

Long-term medication adherence and patient knowledge can be greatly enhanced when therapies are initiated before discharge among patients with AMI. Therefore, recognizing underlying DM during an AMI hospitalization, as opposed to relegating this diagnostic evaluation to the outpatient setting, may have important clinical implications. Patients with AMI are typically hospitalized for 48 to 72 hours, to initiate and titrate cardiac medications and to monitor for mechanical or electrophysiological complications. During this time, patients may be viewed as a captive audience, both more available and more receptive, making this an ideal time for DM education (covering topics such as lifestyle modification, diet, glucose self-monitoring, medication adherence, and DM complications)—an opportunity that is difficult to recreate in the time-pressed outpatient setting. Although DM education

Table 2. Baseline Characteristics of Patients According to Glucose Abnormalities

<table>
<thead>
<tr>
<th></th>
<th>New DM Recognized, n=101</th>
<th>Unrecognized, n=186</th>
<th>Known DM, (n=1339)</th>
<th>No DM, n=2567</th>
<th>PValue*</th>
<th>PValue†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>57.3±9.0</td>
<td>60.0±12.2</td>
<td>60.6±11.7</td>
<td>58.3±12.8</td>
<td>0.049</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, sex</td>
<td>67.3%</td>
<td>69.4%</td>
<td>58.6%</td>
<td>71.0%</td>
<td>0.723</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>White</td>
<td>71.0%</td>
<td>50.0%</td>
<td>58.4%</td>
<td>73.9%</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>24.0%</td>
<td>38.2%</td>
<td>34.2%</td>
<td>19.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5.0%</td>
<td>11.8%</td>
<td>7.4%</td>
<td>6.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>51.5%</td>
<td>47.8%</td>
<td>48.6%</td>
<td>55.8%</td>
<td>0.554</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High school ed or greater</td>
<td>85.0%</td>
<td>78.4%</td>
<td>74.1%</td>
<td>82.1%</td>
<td>0.176</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>31.3±6.1</td>
<td>29.9±5.8</td>
<td>31.6±7.2</td>
<td>28.5±5.8</td>
<td>0.063</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>47.5%</td>
<td>37.5%</td>
<td>29.3%</td>
<td>43.6%</td>
<td>0.103</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>34.7%</td>
<td>48.9%</td>
<td>61.2%</td>
<td>43.3%</td>
<td>0.019</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>61.4%</td>
<td>64.0%</td>
<td>84.2%</td>
<td>57.8%</td>
<td>0.663</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous infarction</td>
<td>12.9%</td>
<td>21.5%</td>
<td>28.2%</td>
<td>17.6%</td>
<td>0.071</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous angioplasty</td>
<td>8.9%</td>
<td>22.6%</td>
<td>25.5%</td>
<td>17.0%</td>
<td>0.003</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous bypass surgery</td>
<td>5.0%</td>
<td>14.0%</td>
<td>18.2%</td>
<td>8.0%</td>
<td>0.018</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>3.0%</td>
<td>9.1%</td>
<td>8.7%</td>
<td>6.4%</td>
<td>0.049</td>
<td>0.013</td>
</tr>
<tr>
<td>Depression</td>
<td>15.8%</td>
<td>11.0%</td>
<td>24.2%</td>
<td>16.7%</td>
<td>0.258</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated GFR, mL/min per 1.73 m²</td>
<td>83.6±29.6</td>
<td>78.4±23.9</td>
<td>69.7±32.2</td>
<td>79.1±24.8</td>
<td>0.107</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST-segment–elevation AMI</td>
<td>47.5%</td>
<td>44.1%</td>
<td>31.4%</td>
<td>49.5%</td>
<td>0.576</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak troponin, ng/dL</td>
<td>40.6±133.7</td>
<td>28.2±85.5</td>
<td>22.2±71.5</td>
<td>32.0±70.9</td>
<td>0.343</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivessel disease, ≥2 vessels</td>
<td>49.0%</td>
<td>54.2%</td>
<td>60.7%</td>
<td>44.9%</td>
<td>0.413</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV systolic dysfunction</td>
<td>24.8%</td>
<td>22.2%</td>
<td>21.6%</td>
<td>16.9%</td>
<td>0.602</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c, core laboratory; %</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean±SD</td>
<td>8.6±2.1</td>
<td>6.9±0.8</td>
<td>8.1±2.1</td>
<td>5.7±0.4</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median, IQR</td>
<td>7.6 (6.8–10.4)</td>
<td>6.7 (6.5–6.9)</td>
<td>7.5 (6.6–9.3)</td>
<td>5.7 (5.4–5.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute range</td>
<td>(6.5–16.5)</td>
<td>(6.5–12.3)</td>
<td>(4.2–16.9)</td>
<td>(3.1–6.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6.5%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>21.6%</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.5–6.9%</td>
<td>27.3%</td>
<td>76.7%</td>
<td>14.6%</td>
<td>0.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0–7.9%</td>
<td>28.3%</td>
<td>18.9%</td>
<td>21.5%</td>
<td>0.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥8%</td>
<td>44.4%</td>
<td>4.4%</td>
<td>42.3%</td>
<td>0.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>174.5±60.4</td>
<td>134.9±40.6</td>
<td>180.6±78.9</td>
<td>112.1±24.3</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin, μIU/mL</td>
<td>19.6±20.6</td>
<td>21.6±25.4</td>
<td>21.3±36.9</td>
<td>16.4±24.2</td>
<td>0.606</td>
<td>0.001</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>196.0±72.4</td>
<td>178.2±46.9</td>
<td>173.6±59.1</td>
<td>175.6±45.5</td>
<td>0.014</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>240.1±445.0</td>
<td>154.4±127.4</td>
<td>178.3±227.8</td>
<td>136.6±99.1</td>
<td>0.017</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>36.3±10.7</td>
<td>41.3±13.2</td>
<td>40.3±12.8</td>
<td>42.5±14.8</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL-C, mg/dL</td>
<td>116.0±36.0</td>
<td>108.0±39.6</td>
<td>99.4±44.7</td>
<td>106.6±40.1</td>
<td>0.108</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin; HDL-C, high density lipoprotein-cholesterol; IQR, interquartile range; LDL-C, low density lipoprotein-cholesterol; and LV, left ventricular.

*Pair-wise comparison between recognized and unrecognized new DM.
†ANOVA comparison across the 4 groups.
is an on-going process and ideally provided multiple times to patients as inpatients and outpatients. Studies have shown a gross underutilization of DM education, particularly in vulnerable populations, making it important to provide to patients whenever possible during the AMI hospitalization. In addition, patients with AMI are often discharged on several new medications, particularly those with newly diagnosed coronary artery disease. This also creates an opportune time for initiating glucose-lowering therapies (when necessary)—to improve patient knowledge about the medications and the likelihood of long-term adherence, which has been shown to be greatly enhanced if the medications are started during the acute hospitalization. Furthermore, initiation of metformin at the time of DM diagnosis, even in patients with mild DM (ie, HbA1c <7%), has been shown to reduce the rate of metformin failure, presumably through preservation of β-cell function. Finally, recognition of DM during the AMI hospitalization can allow for earlier referral to endocrinologists (for patients with poorly controlled DM), which can permit a greater depth of outpatient DM education and likely a quicker path to improved glycemic control.

Beyond the implications on glycemic control and potentially modulating long-term microvascular complications by earlier diagnosis and management of DM, the recognition of DM in the setting of an AMI has potential implications on the cardiac care of these patients as well. During the hospitalization for an AMI, for example, multiple interventional and pharmacological treatments are provided, and the choices made among these various treatments are often influenced by the presence of concomitant DM. For example, an AMI patient with multivessel disease and DM may be preferentially treated with bypass graft surgery instead of multivessel stenting. In addition, multiple pharmacological treatment decisions during the AMI are potentially influenced by the presence or absence of DM, including initiation of angiotensin-converting enzyme inhibitors in the AMI patient with normal left ventricular function, selection of a β-blocker that is metabolically favorable, addition of aldosterone inhibitors in patients with left ventricular dysfunction in the absence of clinical heart failure, or use of more potent antiplatelet agents (eg, prasugrel or ticagrelor). So, at multiple steps during the AMI hospitalization, the diagnosis of concomitant DM has the potential to influence many key treatment decisions during the AMI, making the prompt recognition of underlying DM important beyond the long-term implications on glycemic control.

Standardized, universal testing of patients for DM during an AMI hospitalization would also identify the substantial proportion of patients with pre-DM (eg, HbA1c, 5.7%–6.4%). Although not requiring as intensive of interventions as patients with newly diagnosed DM, these patients can also benefit from DM and nutrition education and could even be considered for metformin therapy, as recommended by the American Diabetes Association. In addition, use of DM-friendly medications might also be selectively chosen in these patients with evidence of insulin resistance to delay the progression to overt DM. We have previously shown that in 3 patients with AMI have pre-DM, most of whom do not have overwhelming hyperglycemia and are likely unaware of this diagnosis. Screening all AMI patients with an HbA1c could therefore result in important, novel, and actionable information for a substantial proportion of patients with AMI.

### Previous Studies

Previous studies evaluating the prevalence of underlying DM that had been previously undiagnosed among patients with coronary artery disease have found higher absolute proportions with previously undiagnosed DM—with estimates of 20% to 30% of such patients. The reason for this discrepancy is likely 2-fold. First, these previous studies relied on oral glucose tolerance testing, which is known to be more sensitive for detecting metabolic abnormalities than the HbA1c level. Second, the prevalence of known DM among the patients with AMI was higher in our study than in the previous studies, which cited rates of established DM of 15% to 30%. As such, the total prevalence of DM (prevalence plus incidence) was 35% to 50% in previous studies, which is not dissimilar from our finding of 39%. This suggests proportionately greater pre-existing DM, likely reflective of the increasing prevalence of and greater outpatient screening for DM in the US during the previous decade.

### Limitations

There are several potential limitations to our study that are important to acknowledge. First, not all patients had an HbA1c level available for analysis and required categorization based on fasting and random glucose measurements, which, as discussed, has known drawbacks in the setting of an AMI. However, this approach has been previously validated, and the results of our sensitivity analysis were nearly identical to the main analysis, increasing our confidence in the alternative DM diagnoses. Second, we defined DM recognition as the initiation of a DM medication, provision of DM education during hospitalization, or documentation of a discharge diagnosis code. It is possible that there were some patients where the diagnosis of DM was indeed recognized by the physician, and this information was shared with the patient or their outpatient clinician(s) without any other intervention or documentation in the chart. The marked discrepancy, however, in the eventual initiation of
glucose-lowering therapy suggests that this was likely not the prevailing strategy in these individuals.

Third, TRIUMPH was conducted during 2005–2008, and the HbA1c threshold for diagnosis of DM of ≥6.5% was not officially recommended until 2009, although there was clear evidence of increased risk of microvascular complications above this threshold before TRIUMPH.29 Furthermore, it is unclear how screening practices have changed over time, with the selective screening recommendations in the scientific statement from the American Heart Association in 2008.11 Understanding whether these publications affected rates of testing and recognition (both during the acute hospitalization and during follow-up) requires further study. In addition, case finding of DM in the outpatient setting (ie, before and after the AMI hospitalization) may also have changed over time,28 decreasing the numbers of patients with underlying DM who remain unrecognized. However, it is important to document where we are, in terms of screening and recognition rates, so as to know if things are improving over time with greater recognition of DM or possible future changes in the AMI guidelines. Fourth, how an earlier recognition of DM during the AMI hospitalization affects both macrovascular treatments, and microvascular outcomes (via earlier treatment of hyperglycemia) during follow-up is not known. As most of the large clinical trials establishing differential benefit of cardiovascular treatments in patients with DM enrolled patients with longer durations of and more severe forms of DM, their effect in patients with milder forms of DM are not definitively known. However, many of these treatments have been shown in smaller studies to be also beneficial in patients with prediabetes.30–32 Finally, although TRIUMPH represents 24 diverse US centers, including both academic and nonacademic hospitals, it is not known if the incidence of DM and the frequency of its recognition would be similar at other US hospitals or internationally. However, this represents the largest study to date in the US population and provides, at least, a reasonable estimate as to these proportions in a contemporary AMI population.

Conclusions
Among AMI patients without a previous diagnosis of DM, 1 in 10 have underlying DM. Recognition of DM remains suboptimal, with only one third of patients with underlying DM being recognized as having DM by the treating physician. Given its frequency and therapeutic implications, including but extending beyond the initiation of glucose-lowering treatment, consideration should be given to screening all patients with AMI for DM during hospitalization. Inexpensive, ubiquitous, and endorsed as an acceptable screen for DM, HbA1c testing should be considered for this purpose.

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Disclosures
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References


Recognition of Incident Diabetes Mellitus During an Acute Myocardial Infarction

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