ORIGINAL RESEARCH

Association of Diabetes Mellitus With Health Status Outcomes in Young Women and Men After Acute Myocardial Infarction: Results From the VIRGO Study

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Background—Diabetes mellitus increases the risk of mortality after acute myocardial infarction (AMI). However, little is known about the association of diabetes mellitus with post-AMI health status outcomes (symptoms, functioning, and quality of life) in younger adults.

Methods and Results—We investigated the association between diabetes mellitus and health status during the first 12 months after AMI, using data from 3501 adults with AMI (42.6% with diabetes mellitus) aged 18 to 55 years enrolled in the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study. Health status was measured with Seattle Angina Questionnaire (SAQ), 12-item Short-Form Health Survey, and EuroQol-Visual Analogue Scale at baseline hospitalization, 1-month, and 12-months post-AMI. At baseline, patients with diabetes mellitus had significantly worse SAQ-angina frequency (81±22 versus 86±19), SAQ-physical limitations (77±28 versus 85±23), SAQ-quality of life (55±25 versus 57±23), 12-item Short-Form Health Survey mental (44±13 versus 46±12)/physical functioning (41±12 versus 46±12), and EuroQol-Visual Analogue Scale (61±22 versus 66±21) than those without diabetes mellitus. Over time, both groups (with and without diabetes mellitus) improved considerably and the differences in health status scores progressively narrowed (except for 12-item Short-Form Health Survey physical functioning). In the linear-mixed effects models, adjusted for sociodemographics, cardiovascular risk factors, comorbidities, clinical characteristics, psychosocial factors, healthcare use, and AMI treatment, diabetes mellitus was associated with worse health status at baseline but not after discharge, and the association did not vary by sex.

Conclusions—At baseline, young adults with diabetes mellitus had poorer health status than those without diabetes mellitus. After AMI, however, they experienced significant improvements and diabetes mellitus was not associated with worse angina, SAQ-physical limitations, mental functioning, and quality of life, after adjustment for baseline covariates.

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Key Words: acute myocardial infarction • angina • diabetes mellitus • patient-reported outcomes • quality of life

Young adults (aged <55 years) with diabetes mellitus have a 6- to 14-fold increased risk of acute myocardial infarction (AMI) and higher mortality after AMI compared with age-matched individuals without diabetes mellitus.[1] Although diabetes mellitus is present in ≈25% of young patients with AMI,[2] its influence on health status outcomes (symptoms, functioning, quality of life)[3] in young women and men following AMI is unknown. Furthermore, whether trajectories

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Accompanying Tables S1 through S3 and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.010988

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Clinical Perspective

What Is New?

- This study is the first to compare changes of health status outcomes (symptoms, functioning, and quality of life) between young acute myocardial infarction (AMI) patients (18–55 years) with and without diabetes mellitus during a 12-month follow-up, and to explore whether the association between diabetes mellitus and post-AMI health status varies by sex.
- Young adults with diabetes mellitus, regardless of sex, had a higher risk of worse health status before and during AMI hospitalization, compared with patients without diabetes mellitus.
- After AMI, young adults with diabetes mellitus experienced rapid health status recovery, and their health status was similar to patients without diabetes mellitus by 1 year.

What Are the Clinical Implications?

- The study findings suggest that current guidelines for the management of AMI seem to be equally effective in young adults with and without diabetes mellitus.
- Increasing access to and use of quality health care may lead to improved post-AMI symptoms, functioning, and quality of life in young adults with diabetes mellitus.

of health status change over the first year after AMI differ between young adults with and without diabetes mellitus has not yet been reported.

The experience of life after AMI is of paramount importance for all, but especially for younger adults because they have higher survival rates than older adults after AMI,[4] and their health status can be improved by aggressive management, such as anti-anginal therapy or revascularization.[5] For AMI patients with diabetes mellitus, health status is not only a strong predictor of survival,[6] but is also associated with adherence to self-care and diabetes mellitus management.[5,7] As a result, assessments of young patients' symptoms, functioning, and quality of life after AMI are essential to understanding how AMI or its treatment affects their lives.[3] Also, identifying differences in health status change over time, between patients with and without diabetes mellitus, is needed to track response to treatment and to determine if those with diabetes mellitus comprise a subgroup of the AMI population who may benefit from additional interventions.

To address these knowledge gaps, we used data from the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study,[8] a prospective observational study of young women and men (aged 18–55 years) hospitalized with AMI, to investigate the association between diabetes mellitus and health status outcomes, including angina frequency, functional status (disease-specific physical limitation and general mental and physical functioning), and quality of life (disease-specific and general), within the first 12 months following AMI. The specific aims were to: (1) examine the association of diabetes mellitus with health status outcomes during the 12-month period after AMI in young adults, and whether the association varies by sex; and (2) to assess differences between young AMI patients with and without diabetes mellitus in trajectories of health status from baseline to 12-month follow-up. We investigated these aims with and without adjustment for sociodemographics, cardiovascular risk factors, comorbidities, clinical characteristics of AMI, psychosocial factors, healthcare use, and AMI treatment.

Methods

Participants and Study Design

Between August 2008 and December 2012, 3501 patients aged 18 to 55 years hospitalized with AMI across 103 US and 24 Spanish hospitals were enrolled in the VIRGO study. The details of the study design and data collection protocols have been published previously.[8] The data, analytic methods, and study materials will be made available to other researchers if they provide funding support for deidentification of protected health information in the study and assurances not to share the database on their own.

In brief, VIRGO was designed to identify factors that contributed to worse outcomes among young women with AMI. Women and men were enrolled using a 2:1 ratio, respectively. Every attempt was made to recruit consecutive young female patients with AMI. After enrolling 2 women, the next man with an AMI was enrolled. The enrolled and non-enrolled patients had similar demographic characteristics,[9] and the demographic and clinical characteristics of enrolled patients were comparable with those enrolled in the National Inpatient Sample of AMI.[2] Participants were required to have a rise of cardiac biomarkers (preferably troponin) with at least 1 value >99th percentile of the upper reference limit within 24 hours of admission, and had to meet at least 1 criterion for acute myocardial ischemia (symptoms of ischemia, ECG changes indicative of new ischemia, or other evidence of myocardial necrosis).[8] Only patients who presented to participating hospitals, or who were transferred within the first 24 hours, were included to ensure that the primary clinical decision making was being performed at the enrolling site.[8] Participants were excluded if they had elevated cardiac markers as a complication of elective coronary revascularization, were previously enrolled in VIRGO, did not speak English or Spanish, were unable to provide informed consent, were

unable to be contacted for follow up, had an AMI attributable to physical trauma, or were currently a prisoner.[8]

Data Collection and Variables

Patient characteristics

Baseline characteristics including sociodemographics, cardiovascular risk factors, comorbidities, clinical characteristics, psychosocial factors, healthcare use, and AMI treatment were collected through medical record abstraction and in-person interviews during the index AMI admission.[8] In-hospital complications and mortality after AMI were also obtained by reviewing patients' medical records. Follow-up data were collected by trained research staff at baseline, and at 1 and 12 months following the AMI. At 1-month follow-up, fasting blood was drawn from all U.S. participants and was analyzed for glycated hemoglobin (HbA1c) at a specified laboratory (Quest Diagnostics, USA). Each participating institution obtained Institutional Research Board approval, and all participants provided informed consent for in-hospital and follow-up data collection.

Sociodemographics included age, sex, race, Hispanic ethnicity (Yes/No), marital status, education, employment status, and annual household income. Cardiovascular risk factors included a family history of cardiovascular disease, hypertension, hypercholesterolemia, smoking 30 days before admission, sleep apnea, and body mass index $\geq$30 kg/m^2. Comorbidities included renal dysfunction, heart failure, stroke, depression, alcohol abuse, prior AMI, and prior primary percutaneous coronary intervention. Clinical characteristics of AMI included angiographic documentation of coronary occlusion $\geq$50%, AMI symptom presentation at admission, ST-segment–elevation myocardial infarction, initial systolic and diastolic blood pressure, heart rate, peak troponin, left ventricular ejection fraction <40%, whether the patient presented to the hospital >6 hours after symptom onset, and GRACE (Global Registry of Acute Coronary Events) risk score.

Diabetes mellitus-related characteristics were collected from the medical record and baseline self-report, and included HbA1c recorded at admission or within 3 months before admission and at 1-month follow-up, admission glucose level, peak creatinine level, chart documented type of self-reported diabetes mellitus (type 1 or type 2), self-reported diabetes mellitus treatment (none, diet only, insulin, or oral hypoglycemic drugs), and self-reported diabetes mellitus-related complications (kidney disease, retinopathy, neuropathy, amputation, and other complications).

Baseline psychosocial factors included social support, stress, and depressive symptoms. Social support was measured using the 7-item ENRICHD Social Support Instrument, derived from questions on the Medical Outcomes Survey.[10] The social support score was obtained by summing all 7 items, with higher scores indicating better social support.[10] Stress was measured with the 14-item Perceived Stress Scale.[11] Individual items were then summed for a total Perceived Stress Scale score, with higher scores indicating a higher level of perceived stress.[11] Depressive symptoms were measured with the 9-item version of the Patient Health Questionnaire.[12] Higher Patient Health Questionnaire-9 scores represented worse depression.[12] These questionnaires have well-documented reliability and validity. Healthcare use at baseline was assessed by health insurance (Yes/No) and self-report of difficulty obtaining medical care when needed, medical costs posing an economic burden over the past year, avoiding healthcare services because of cost, and frequently not taking prescribed medication because of cost.

AMI treatment variables included coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), diagnostic angiography, aspirin at arrival, primary reperfusion (fibrinolytic therapy and primary angioplasty), and discharge medications (aspirin, statin, beta-blocker, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker).

Diagnosis of diabetes mellitus

Because undiagnosed diabetes mellitus is prevalent among individuals with AMI,[13] diabetes mellitus was defined based on multiple criteria at 3 different time-points: (1) baseline: defined as a chart-documented or self-reported history of diabetes mellitus, documentation of HbA1c $\geq$6.5%, or the use of glucose-lowering medications before index admission (except for metformin monotherapy); (2) discharge: a discharge diagnosis of diabetes mellitus or a prescription for glucose-lowering medications (including metformin); or (3) 1-month follow-up: HbA1c $\geq$6.5% or current use of diabetes mellitus medication (individuals with polycystic ovarian syndrome treated with metformin, but without any other evidence to suggest the presence of diabetes mellitus, were classified as not having diabetes mellitus).

Health status outcomes assessment

Disease-specific health status (angina frequency, disease-specific physical limitations, and disease-specific quality of life) was assessed using the Seattle Angina Questionnaire (SAQ). General mental and physical functioning were measured using the 12-item Short-Form Health Survey (SF-12). General quality of life was assessed using the EuroQol-5 Dimensions (EQ-5D)-Visual Analogue Scale (EQ-VAS). Although the EQ-VAS evaluated the respondent's current health state[14], the SAQ and SF-12 addressed health status over the 4 weeks preceding the interview.[15,16]

The SAQ is a 19-item validated questionnaire used to measure disease-specific health status for patients with coronary artery disease.[15] The SAQ contains 5 clinically important domains

including angina frequency, physical limitations, quality of life, angina stability, and treatment satisfaction. In this study, we focused on the angina frequency, physical limitations, and quality of life domains of SAQ. For each domain, the scores range from 0 to 100, with higher scores indicating better functioning (eg, fewer angina symptoms, fewer physical limitations, and better quality of life). A mean difference ≥5 points in each of the domains is considered clinically meaningful.[15,17]

Both the SF-12 and the EQ-VAS are reliable and valid measures of general health and quality of life respectively, and their scores range from 0 to 100, with higher ratings being more favorable.[14,16] The SF-12 assesses overall physical and mental functioning using the mental health and physical health component scale scores.[16] Generally, the minimum clinically important differences in SF-12 scores are 3 to 5 points.[18]

The EQ-VAS offers a simple way to determine general quality of life on a 20-cm vertical visual analogue scale, whereby 0 indicates "the worst health you can imagine," and 100 indicates "the best health you can imagine."[14] The minimum clinically meaningful differences in EQ-VAS for patients with cardiovascular disease has yet to be determined.[19,20]

Statistical Analysis

Baseline characteristics for patients with and without diabetes mellitus were compared using Chi-squared tests, Fisher-exact tests, *t*-tests, and Wilcoxon-signed rank tests, as appropriate. Mean health status scores at baseline, 1 month, and 12 months after AMI were separately compared using t-tests and were plotted for patients with and without diabetes mellitus. Exploratory analyses were also performed to compare in-hospital complications, in-hospital mortality, and mortality at 1-month and 12-months follow-up between patients with and without diabetes mellitus (Table S1).

To investigate the association of diabetes mellitus with health status during the 12-month period after AMI, we used linear-mixed effects (LME) regression models to fit the repeated measurements for each health status outcome separately. This approach allowed us to study changes in health status over time for patients with and without diabetes mellitus, and simultaneously examine individual-specific (within-person) and between-person (heterogeneity) characteristics that contribute to the variability in health status trajectories.[21]

In our LME models, random-effects terms included the intercept (to account for the within-person effect of the repeated health status measures) and the slope of time (to account for the within-person clustering over time). Each patient's diabetes mellitus status (Yes/No) and follow-up time points (time 1: baseline; time 2: 1 month; time 3: 12 months) were included as fixed-effects. The reference group was patients without diabetes mellitus.

First, we examined diabetes mellitus status alone with the random-effects for the intercept in the unadjusted model. We then fitted a basic model (Adjusted #1) that included the main effect of diabetes mellitus status and time, with the random-effects terms. The second adjusted model (Adjusted #2) added sex to Adjusted #1. Interactions between diabetes mellitus, sex, and time were explored in Adjusted #2 and were included when significant. If the interaction between diabetes mellitus and sex was significant in Adjusted #2, we performed the following sequential adjustment (#3–#9) separately for men and women. We constructed adjusted models #3 to #9 by adding the following variables to Adjusted #2 in order: (1) other sociodemographics; (2) cardiovascular risk factors; (3) comorbidities; (4) AMI clinical characteristics; (5) psychosocial factors; (6) healthcare use; and (7) AMI treatment.

We tested whether the association between diabetes mellitus and each post-AMI health status outcome differed between young women and men by adding the interaction of diabetes mellitus and sex in the LME models #2 and #9 (fully adjusted). We reported parameter estimates (PE), and the 95% CI of diabetes mellitus in each LME model, as well as *P*-values for the interaction terms.

Missing health status data for patients with and without diabetes mellitus are shown in Figure S1, with < 23% of patients missing any health status outcome. The LME models are sufficient to account for missing response and covariate data that are missing at random.[22] A comparison of baseline characteristics between patients who completed the interview at 12 months and those lost to follow-up have been reported previously.[20] Missing covariates were minimal (<5% of study population), and were imputed to the most common category for categorical variables and the median for continuous variables. We excluded type and treatment of diabetes mellitus variables from the primary analyses because a large portion of patients had unknown diabetes mellitus type (43.3%). The treatment of diabetes mellitus variable was not reliable as it was self-report, and thus was not used to impute diabetes mellitus type. We performed additional exploratory analyses assessing the influence of diabetes mellitus type on health status outcomes. All analyses were performed with SAS 9.3. (SAS Institute Inc, Cary, NC), and statistical significance was defined as a $P<0.05$ for 2-sided tests.

Results

Baseline Characteristics Stratified by Mellitus Status

The overall prevalence of diabetes mellitus was 42.6%. Differences between patients with and without diabetes mellitus in baseline characteristics are presented in Table 1. Patients with diabetes mellitus were older, more frequently

Table 1. Comparison of Baseline Characteristics Between AMI Patients With and Without Diabetes Mellitus

Characteristics	With Diabetes Mellitus (n=1493, 42.64%)	Without Diabetes Mellitus (n=2008, 57.36%)	*P* Value
Sociodemographics			
Age, year (median, IQR)	49.00 (8.00)	48.00 (8.00)	0.0002
Women	1079 (72.27%)	1270 (63.25%)	0.0001
Race			
White	1093 (73.21%)	1649 (82.12%)	0.0001
Black	302 (20.23%)	248 (12.35%)	
Others	98 (6.56%)	111 (5.53%)	
Hispanic (yes/no)	128 (8.57%)	141 (7.02%)	0.1581
Marital status			
With partner	788 (52.78%)	1241 (61.80%)	<0.0001
Without partner	692 (46.35%)	742 (36.95%)	
Unknown	13 (0.87%)	25 (1.25%)	
Education status			
Less than high school	76 (5.09%)	176 (8.76%)	0.0003
Some high school	633 (42.40%)	784 (39.04%)	
More than high school	784 (52.51%)	1048 (52.19%)	
Employment status			
Working full-time	666 (43.94%)	1131 (56.82%)	<0.0001
Working part-time	154 (10.31%)	216 (10.76%)	
Not working	683 (45.75%)	661 (32.92%)	
Household income			
<$30 000	746 (49.97%)	762 (37.95%)	<0.0001
$30 000 to $69 999	401 (26.86%)	619 (30.83%)	
≥$70 000	346 (23.17%)	627 (31.23%)	
CVD risk factors			
Family history of CVD	1110 (74.35%)	1395 (69.47%)	0.0035
History of hypertension	1121 (75.08%)	1096 (54.58%)	<0.0001
History of hypercholesterolemia	1354 (90.69%)	1648 (82.07%)	<0.0001
Smoking within past 30 d	844 (56.53%)	1241 (61.80%)	0.0027
Sleep apnea	112 (7.50%)	49 (2.44%)	<0.0001
Body mass index >30 kg/m^2	942 (63.09%)	767 (38.20%)	<0.0001
Other comorbidities			
History of renal dysfunction	219 (14.67%)	143 (7.12%)	<0.0001
History of heart failure	111 (7.43%)	30 (1.49%)	<0.0001
History of prior stroke/TIA	92 (6.16%)	55 (2.74%)	<0.0001
History of depression	667 (44.68%)	731 (36.40%)	<0.0001
History of alcohol abuse	79 (5.29%)	152 (7.57%)	0.0190
Prior MI	301 (20.16%)	242 (12.05%)	<0.0001
Prior PCI	295 (19.76%)	213 (10.61%)	<0.0001

Continued

Table 1. Continued

Characteristics	With Diabetes Mellitus (n=1493, 42.64%)	Without Diabetes Mellitus (n=2008, 57.36%)	*P* Value
Clinical charcteristics of AMI			
Coronary occlusion ≥50% (documented by coronary angiography)			
Yes	1290 (86.40%)	1637 (81.52%)	<0.0001
No	106 (7.10%)	244 (12.15%)	
Unknown	97 (6.50%)	127 (6.32%)	
Atypical chest pain	289 (19.36%)	335 (16.68%)	0.0409
ST-segment–elevation MI	734 (49.16%)	1077 (53.64%)	0.0088
Initial systolic blood pressure, median (IQR)	144.00 (40.00)	140.00 (37.00)	0.0002
Initial diastolic blood pressure, median (IQR)	86.00 (27.00)	87.00 (24.00)	0.9570
Initial heart rate, median (IQR)	85.00 (25.00)	78.00 (23.00)	<0.0001
Peak troponin, median (IQR)	5.95 (22.19)	8.11 (31.52)	0.0039
Ejection fraction <40%	179 (12.42%)	189 (9.63%)	0.0096
Time to presentation >6 hours	699 (47.07%)	767 (38.29%)	<0.0001
GRACE scores			
GRACE 0 to 99	1290 (86.4%)	1846 (91.93%)	<0.0001
GRACE 100 to 127	149 (9.98%)	112 (5.58%)	
GRACE 128 to 263	26 (1.74%)	9 (0.45%)	
Unknown	28 (1.88%)	41 (2.04%)	
Diabetes mellitus-related characteristics			
HbA1c at admission or within the past 3 months before admission, median (IQR)	7.80 (3.90)	5.60 (0.50)	<0.0001
1-month HbA1c, median (IQR)	7.03 (1.54)	6.00 (0.52)	<0.0001
Initial glucose, median (IQR)	169.50 (144.00)	117.00 (36.00)	<0.0001
Peak glucose, median (IQR)	200.00 (165.00)	127.00 (38.00)	<0.0001
Peak creatinine, median (IQR)	0.95 (0.30)	0.90 (0.30)	0.0012
Types of diabetes mellitus			
Type I	104 (6.97%)	NA	NA
Type II	742 (49.70%)	NA	
Unknown	647 (43.33%)	NA	
Treatment of diabetes mellitus			
None	105 (7.03%)	NA	NA
Diet	245 (16.41%)	NA	NA
Insulin	367 (24.58%)	NA	NA
Oral hypoglycemic drugs	445 (29.81%)	NA	NA
Unknown	331 (22.17%)	NA	NA
Diabetes mellitus-related complications			
Kidney disease	80 (5.36%)	NA	NA
Retinopathy	69 (4.62%)	NA	NA
Neuropathy	120 (8.04%)	NA	NA
Amputation	26 (1.74%)	NA	NA
Other complications	31 (2.08%)	NA	NA
Unknown	1167 (78.16%)	NA	NA

Continued

Table 1. Continued

Characteristics	With Diabetes Mellitus (n=1493, 42.64%)	Without Diabetes Mellitus (n=2008, 57.36%)	*P* Value
Psychoscial factors			
Social support via ESSI, mean (SD)	21.10 (4.64)	21.63 (4.39)	0.0007
Stress via PSS, mean (SD)	26.66 (9.92)	25.18 (9.55)	<0.0001
Depressive symptom via PHQ-9, mean (SD)	8.80 (6.66)	6.94 (6.07)	<0.0001
Healthcare use			
Health insurance			
Insured	1168 (78.23%)	1631 (81.23%)	0.0457
How difficult is it for you to get medical care when needed?			
Extremely difficult	166 (11.12%)	172 (8.57%)	0.0133
Some difficult	251 (16.81%)	310 (15.44%)	
Little/no difficult	1076 (72.07%)	1526 (75.99%)	
Have your medical costs been an economic burden to you over the past year?			
Severe burden	259 (17.35%)	204 (10.16%)	<0.0001
Some burden	327 (21.90%)	352 (17.53%)	
Little/no burden	907 (60.75%)	1452 (72.31%)	
Avoided healthcare services because of cost (Yes/No)	539 (36.10%)	517 (25.75%)	<0.0001
How often have you not taken a medication that your doctor prescribed because of the cost?			
Always	82 (5.49%)	67 (3.34%)	<0.0001
Sometimes	309 (20.70%)	251 (12.50%)	
Rarely to never	1102 (73.81%)	1690 (84.16%)	
AMI treatment			
Coronary revascularization (PCI/CABG)	1256 (84.13%)	1595 (79.43%)	0.0004
Diagnostic angiography	1412 (94.57%)	1900 (94.62%)	0.9516
Aspirin at arrival	1418 (94.98%)	1939 (96.56%)	0.0132
Primary reperfusion			
Fibrinolytic therapy	72 (4.82%)	127 (6.32%)	0.0103
Primary angioplasty	693 (46.42%)	996 (49.60%)	
None	618 (41.39%)	746 (37.15%)	
Unknown	110 (7.37%)	139 (6.92%)	
Discharge medications			
Aspirin at discharge	1426 (95.51%)	1948 (97.01%)	0.0606
Statin prescribed	1385 (92.77%)	1827 (90.99%)	0.1206
Beta-blocker prescribed	1364 (91.36%)	1779 (88.60%)	0.0179
ACE inhibitors or ARB prescribed	1038 (69.52%)	1193 (59.41%)	<0.0001

ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; CVD, cardiovascular disease; ESSI, ENRICHD Social Support Instrument; GRACE, Global Registry of Acute Coronary Events (higher scores indicating higher risk of death); HbA1c, glycated hemoglobin; IQR, interquartile range; MI, myocardial infarction; NA, information not available; PCI, percutaneous coronary intervention; PHQ-9, Patient Health Questionnaire-9; PSS, Perceived Stress Scale.

women, non-white, living without a partner, unemployed, and had an annual household income of <$30 000, as compared with patients without diabetes mellitus. In terms of cardiovascular risk factors and comorbidities, patients with diabetes mellitus (versus without diabetes mellitus) were significantly more likely to have a family history of cardiovascular disease, a history of hypertension, hypercholesterolemia, sleep apnea, body mass index >30 kg/m^2, renal dysfunction, heart failure, prior stroke/transient ischemic attack, depression, prior AMI, and prior percutaneous coronary intervention, but were less likely to smoke or to have a history of alcohol abuse.

During AMI hospitalization, patients with diabetes mellitus were less likely to present with ST-segment elevation myocardial infarction (49.2% versus 53.6%, $P<0.01$), but were more likely to have an ejection fraction <40% (12.4% versus 9.6%, $P<0.01$), and more frequently presented to the hospital >6 hours after symptom onset (47.1% versus 38.3%, $P<0.001$) than patients without diabetes mellitus. Patients with diabetes mellitus were less likely to receive reperfusion therapy ($P=0.01$) [fibrinolytic therapy (5.2% versus 6.8%) and primary angioplasty (50.1% versus 53.3%)].

There were multiple baseline psychosocial and healthcare use differences between patients with and without diabetes mellitus. Patients with diabetes mellitus (versus without diabetes mellitus) reported higher stress and depressive symptoms. They also had more difficulties in getting medical care when needed ($P=0.01$), and they were more likely to experience economic burden because of medical cost ($P<0.001$), more frequently avoided healthcare services because of cost ($P<0.001$), and more often had not taken a medication that their doctor prescribed because of cost ($P<0.001$).

Post-AMI Mortality

Post-AMI mortality was low, regardless of diabetes mellitus status (Table S1). However, 1-year mortality was higher in young adults with diabetes mellitus (2.7% versus 1.6%, $P=0.03$).

Health Status Stratified by Diabetes Mellitus Status

Young adults with diabetes mellitus had significantly worse SAQ-angina frequency, general physical functioning, and general quality of life scores at baseline (ie, in the 4 weeks preceding their AMI), 1-month and 12-months after AMI, compared with those without diabetes mellitus (Table 2). However, their disease-specific physical limitations and disease-specific quality of life scores were not statistically significantly different from patients without diabetes mellitus at 1- and 12-months after AMI. Patients with diabetes mellitus experienced significantly worse general mental functioning

Table 2. Comparison of Health Status Between AMI Patients With and Without Diabetes Mellitus

Health Status	With Diabetes Mellitus (n=1493, 42.64%) Mean (SD)	Without Diabetes Mellitus (n=2008, 57.36%) Mean (SD)	*P* Value*
Baseline			
SAQ-angina frequency	81.43 (22.17)	85.84 (18.94)	<0.0001
SAQ-physical limitations	76.76 (27.79)	84.56 (22.93)	<0.0001
SAQ-quality of life	55.34 (25.48)	57.48 (22.84)	0.0106
SF-12 mental functioning	44.10 (12.65)	46.36 (12.37)	<0.0001
SF-12 physical functioning	41.25 (12.17)	45.84 (11.65)	<0.0001
EQ-VAS	61.39 (22.25)	66.34 (20.62)	<0.0001
1-Month			
SAQ-angina frequency	88.09 (18.33)	89.51 (17.27)	0.0247
SAQ-physical limitations	89.62 (20.13)	89.90 (19.09)	0.6890
SAQ-quality of life	68.13 (25.81)	67.96 (24.57)	0.8553
SF-12 mental functioning	49.67 (10.72)	49.61 (10.85)	0.8927
SF-12 physical functioning	39.52 (11.91)	43.51 (11.28)	<0.0001
EQ-VAS	69.04 (21.65)	71.75 (20.09)	0.0003
12-Mo			
SAQ-angina frequency	90.43 (17.60)	92.06 (19.03)	0.0112
SAQ-physical limitations	91.11 (19.78)	91.87 (17.98)	0.2982
SAQ-quality of life	72.33 (24.00)	72.23 (22.51)	0.9132
SF-12 mental functioning	49.72 (11.12)	50.61 (10.80)	0.0370
SF-12 physical functioning	42.24 (12.78)	46.14 (11.55)	<0.0001
EQ-VAS	71.23 (21.57)	73.61 (20.22)	0.0034

EQ-VAS indicates EuroQol-5 Dimensions Visual Analogue Scale; SAQ, Seattle Angina Questionnaire; SF-12, 12-Item Short-Form Survey; SF-12 MCS, general mental functioning; SF-12 PCS, general physical functioning.

**P* value testing whether the differences between patients with and without diabetes mellitus are statistically significant.

only at baseline and 12-months, but not at 1-month post-AMI. When stratified by diabetes mellitus type, patients with type 1 diabetes mellitus (versus type 2) had significantly poorer baseline general quality of life and disease-specific physical limitations and quality of life at 1-month (Table S2).

Independent Association Between Diabetes Mellitus and Post-AMI Health Status

In the unadjusted LME models, diabetes mellitus was associated with increased likelihood of angina symptoms, more disease-specific physical limitations, poorer physical and mental functioning, and worse general quality of life over the 12-month follow-up (Table S3: Unadjusted models). In the model including only diabetes mellitus, sex, and time, the interaction between diabetes mellitus and sex was not significant (Adjusted #2: $P>0.05$ for all health status outcomes).

In the adjusted LME models, the relationship between diabetes mellitus and lower general physical functioning score was attenuated, yet remained statistically significant, after accounting for time effects, sex, other sociodemographics, cardiovascular risk factors, comorbidities, AMI clinical characteristics, as well as psychosocial factors, healthcare use, and AMI treatment (Adjusted model #9: −0.67 points, 95% CI: −1.30, −0.08; $P=0.03$ versus Unadjusted: −4.23 points, 95% CI: −4.91, −3.54; $P<0.0001$, Table S3). No interactions between diabetes mellitus, time, and sex were found, suggesting that patients with diabetes mellitus, regardless of sex, experienced consistently poorer physical functioning before and throughout the 12-month period after AMI. Diabetes mellitus was not associated with disease-specific quality of life as per SAQ before or after adjustment (Table S3).

However, the interaction between diabetes mellitus and time was statistically significant for disease-specific (angina frequency, physical limitations) and other general health status outcomes (mental functioning and quality of life), with or without adjustment (Table S3: $P<0.05$ in Adjusted models #2 and #9). When the interaction term between diabetes mellitus and time was added to the analysis, the influence of diabetes mellitus on angina frequency occurred only at baseline with no apparent effect at 12-month follow-up ($P<0.05$ for beta coefficients of diabetes mellitus at time 1, $P>0.05$ for beta coefficients of diabetes mellitus at time 3). Further adjustment for the differences in proportions of patients who had coronary occlusion ≥50% and left ventricular ejection fraction <40% did not explain the greater amount of angina reported by patients with diabetes mellitus at baseline (Table S3).

Similarly, diabetes mellitus was associated with disease-specific physical limitations, worse general mental functioning, and general quality of life only at baseline; these associations diminished over time and were no longer significant at 12 months. Exploratory analysis suggested that further adjustment for diabetes mellitus type did not change these results. However, diabetes mellitus type was associated with disease-specific and general quality of life, and patients with type 1 diabetes mellitus had increased risk for worse post-AMI quality of life compared with those with type 2 diabetes mellitus (Table S3).

As with the analysis in models including only diabetes mellitus, sex, and time, the interaction term between diabetes mellitus and sex was not statistically significant for any of the health status outcomes in the fully adjusted models (Adjusted #9, Table S3). Thus, there was no evidence that the relationship between diabetes mellitus and health status in young adults with AMI varies between women and men (Table S3: *P*-value for the interaction of sex and diabetes mellitus >0.05).

Magnitude of Longitudinal Changes in Health Status Among Patients With and Without Diabetes Mellitus

Although young adults with diabetes mellitus had worse health status at baseline compared with those without diabetes mellitus, the pattern and extent of improvement in SAQ (angina frequency, physical limitation, quality of life), SF-12 (mental functioning), and EQ-VAS (general quality of life) scores differed significantly between those with and without diabetes mellitus (Table S3: *P*-values for the interactions of diabetes mellitus and time <0.05; Figures 1 and 2). Health status in both groups (with and without diabetes mellitus) improved over time. However, those with diabetes mellitus showed a more significant improvement during the first month after AMI, as indicated by the gaps in health status scores between the 2 groups that narrowed by 1 month, and this narrowing persisted at 12 months. At 12 months, many of the differences between patients with and without diabetes mellitus in health status scores were no longer present except for SF-12 physical functioning. The magnitude of changes in SF-12 physical functioning from baseline to 12 months was not statistically different between those with and without diabetes mellitus.

Discussion

In our study of young adults hospitalized with AMI, we found that diabetes mellitus was common, and patients with diabetes mellitus were older, had significantly more comorbidities and psychosocial stressors, compared with those without diabetes mellitus. They also reported significantly greater angina burden, more severe disease-specific physical limitations, poorer physical and mental functioning, and worse general and disease-specific quality of life at baseline

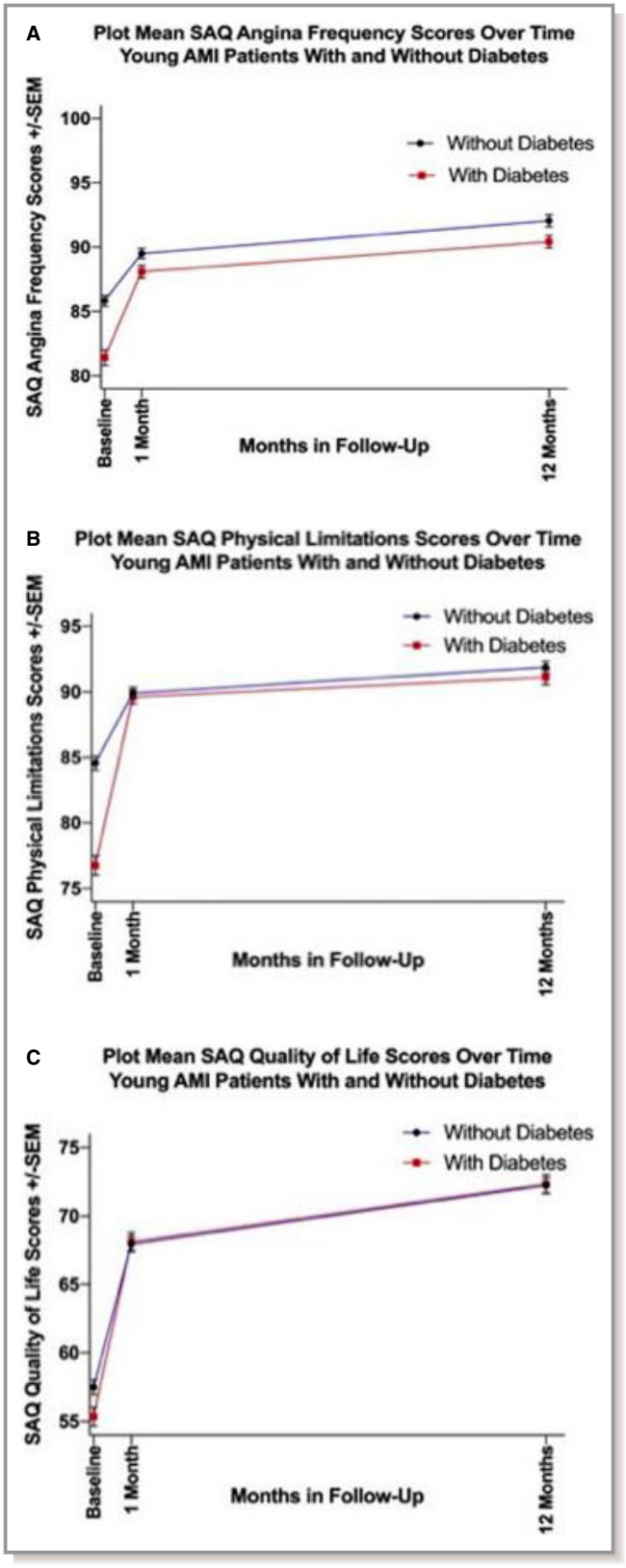

Figure 1. Trends in unadjusted disease-specific health status outcomes (SAQ), stratified by diabetes mellitus status (without diabetes mellitus=blue, with diabetes mellitus=red). **A**, SAQ angina frequency. **B**, SAQ physical limitations. **C**, SAQ quality of life. SAQ indicates Seattle Angina Questionnaire.

hospitalization. The association of diabetes mellitus with worse health status at baseline was not fully explained by differences in sex, other sociodemographics, cardiovascular risk factors, comorbidities, clinical characteristics, psychosocial factors, healthcare use, AMI treatment, or the interactions between diabetes mellitus, sex, and time. However, during the year following AMI, the association between diabetes mellitus and health status outcomes was attenuated and no longer statistically significant at 1- and 12-months post-AMI (except for general physical functioning). The association between diabetes mellitus and poor physical functioning persisted throughout the 12-month period after AMI. Regardless of diabetes mellitus status, young adults demonstrated an improvement in health status from baseline to 12 months following AMI. However, young adults with diabetes mellitus had a rapid recovery, achieving health status improvements that were markedly better than at baseline and similar to those without diabetes mellitus (except for general physical functioning).

In this study, young adults with diabetes mellitus experienced significantly greater angina burden despite adjustment for differences in baseline characteristics between patients with and without diabetes mellitus. Our findings contradicted conventional wisdom that silent ischemia is more common in patients with diabetes mellitus,[23] but this result is consistent with other recent studies.[24,25] While the mechanisms resulting in worse general health status at baseline require further investigation, existing literature suggests that an increased risk burden before AMI admission,[26] a more severe and diffuse nature of the coronary disease,[27] microvascular changes of the heart,[27] and metabolic alterations[28] may play essential roles in the increased angina burden among patients with diabetes mellitus. Significant controversy exists on whether patients with diabetes mellitus experience more angina than those without diabetes mellitus.[29] Our findings are consistent with a recent analysis of the TRIUMPH study on the independent association between diabetes mellitus and angina before AMI.[24] However, Arnold and colleagues reported that diabetes mellitus was associated with significantly increased angina burden as measured by SAQ not only before the index AMI admission but also at 12 months after AMI.[24] Discrepancies between the findings of that study[24] and ours may be related to differences in definitions of diabetes mellitus, the relatively younger population, and a 2:1 (women versus men) ratio in patient recruitment in VIRGO study.

We would expect patients with diabetes mellitus to continue to have poorer health status than those without diabetes mellitus after AMI because diabetes mellitus is often associated with an increased risk of adverse clinical outcomes following discharge.[30] However, AMI appears to act as an equalizer by mitigating the adverse effect of diabetes mellitus on health status. Patients with diabetes mellitus

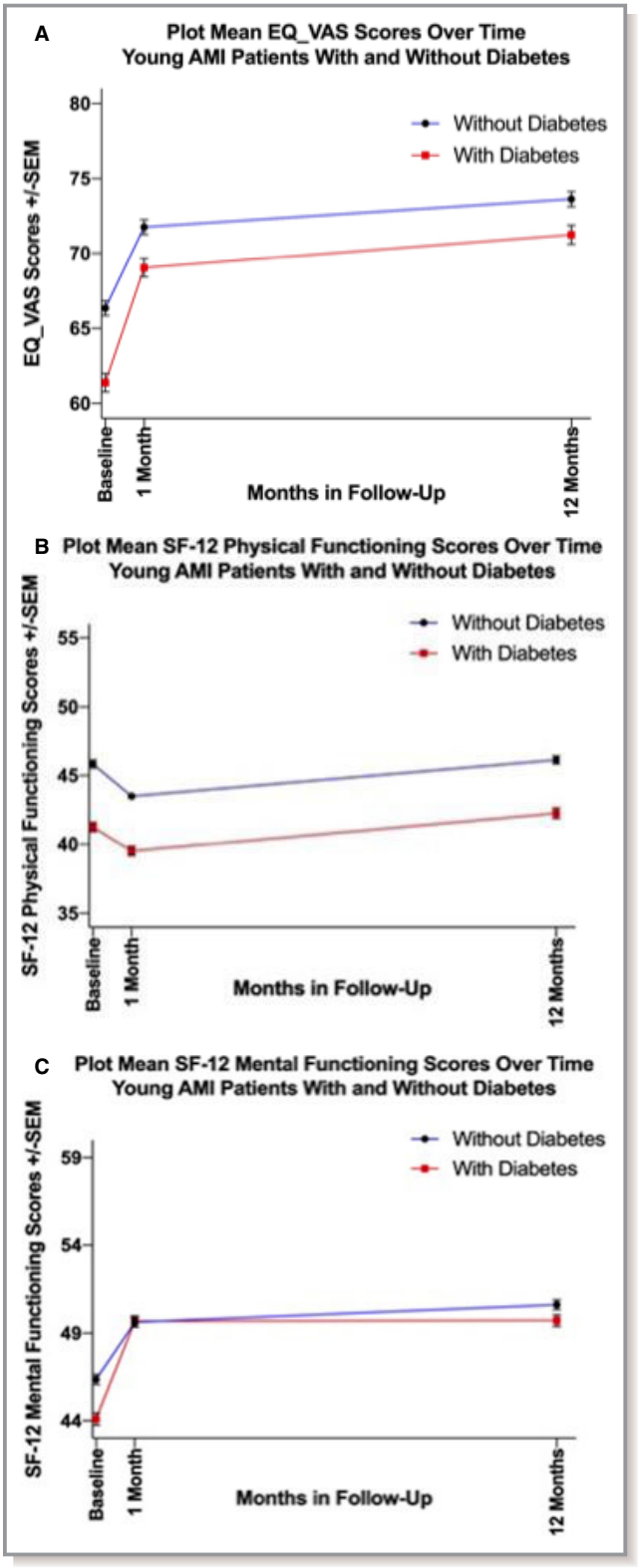

Figure 2. Trends in unadjusted generic health status outcomes (SF-12 & EQ-VAS), stratified by diabetes mellitus status (without diabetes mellitus=blue, with diabetes mellitus=red). **A**, SF-12 mental functioning. **B**, SF-12 physical functioning. **C**, EQ-VAS. EQ-VAS indicates EuroQol-5 Dimensions Visual Analogue Scale; SF-12, 12-Item Short-Form Survey.

demonstrated considerable improvement throughout the 12-month follow-up period. Part of the differences in the magnitude of health status improvement between patients with and without diabetes mellitus may be attributable to differences in healthcare use and AMI treatment received. Indeed, in our study, young adults with diabetes mellitus faced significantly more barriers to health care before AMI hospitalization, and they received aspirin at arrival, fibrinolytic therapy, and primary angioplasty during hospitalization much less frequently than those without diabetes mellitus. However, the use of diagnostic angiography and medications prescribed at discharge (aspirin, statins, beta-blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker) were similar between patients with and without diabetes mellitus, which may have contributed to the improved health status observed in this population. In the 2011 update of the guideline on "Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and Other Atherosclerotic Vascular Disease," the American Heart Association/American College of Cardiology Foundation emphasized tight glycemic control, cardiovascular risk modification, and the use of angiotensin-converting enzyme inhibitor in individuals with diabetes mellitus.[31] There is also convincing evidence that the use of angiotensin-converting enzyme inhibitor, aspirin, beta-blockers, statins, and reperfusion and revascularization procedures are beneficial in AMI patients with and without diabetes mellitus, and could lead to at least a 22% reduction in mortality.[32,33]

In our study, we noticed that there were more patients who received fibrinolytic therapy or primary angioplasty than were identified as having an ST-segment–elevation myocardial infarction. Although fibrinolytic therapy has not been shown to have a beneficial effect on the prognosis when administered to patients with non–ST-segment–elevation myocardial infarction,[34] findings from a large, contemporary real-world study in Sweden showed that early invasive treatment such as percutaneous coronary intervention is associated with lower risk of ischemic outcomes in patients with non–ST-segment–elevation myocardial infarction.[35] Our findings may be related to variations in medical practice in real-world settings. Further studies are needed to carefully examine the association between the type of AMI, diabetes mellitus status, and AMI treatment in the younger population.

In the present study, we found that diabetes mellitus affects the magnitude of the changes differently in disease-specific physical limitations and general physical functioning after AMI. Young adults with diabetes mellitus reported substantial improvement in disease-specific physical limitations from baseline to 1-month follow-up; however, they experienced a significant decline in general physical functioning during the first month. Most studies of the relationship between diabetes mellitus and health status have been cross-sectional and did not

include both disease-specific and generic measures. Our study demonstrates the importance of including both disease-specific and general measures to capture the impact of diabetes mellitus on changes in how daily activities are limited by angina symptoms (disease-specific physical limitations)[15], and the individual's overall physical functioning, role limitations as related to physical problems, bodily pain, and vitality (general physical functioning).[16]

The prevalence of diabetes mellitus in our study (42.6% overall and 45.9% in women) is higher than in most previous studies: 24.5% (mean age: 58.0 years, the percentage of women in the study: 33.4%) by Vaccarino and colleagues.[36] (US), 28.6% (mean age: 61.9 years, women: 32.1%) by Meisinger and colleagues.[37] (Germany), and 22.8% (10.2% study population at age 30–49 years, 45.3% at age 50–69, 44.5% at age 70–89 years; women: 26.9%) by Abbud and colleagues (US).[30] The higher prevalence rate reported here, therefore, could reflect differences in the definition of diabetes mellitus or differences in age or sex distribution of the study populations. Oversampling of women in the VIRGO study may contribute to the higher diabetes mellitus prevalence in our study since there are more women than men with diabetes mellitus.[38] In prior research, the diagnosis of diabetes mellitus has primarily been based solely on medical record documentation[36] or self-report at the time of AMI hospitalization, with no other confirmation of the diagnosis.[30] We defined diabetes mellitus on the basis of standard criteria (HbA1c) in addition to a history of diabetes mellitus in the medical record. It is anticipated that our approach may be less prone to misclassification of diabetes mellitus, and thus less likely to underestimate its prevalence.[36]

The present study did not show that the association between diabetes mellitus and post-AMI health status differed between women and men. Results of prior studies have suggested that diabetes mellitus has a stronger effect on women than men related to clinical outcomes after AMI, particularly for women with heart failure.[39] Because of the low rates of in-hospital complications and mortality in this population, our analysis focused on health status outcomes. However, our study is the first to formally test an interaction between diabetes mellitus and sex in young adults with AMI, with respect to health status outcomes. We are uncertain why a diabetes mellitus-sex interaction was not observed. Additional research is needed to better understand the sex-specific association between diabetes mellitus and health status in young patients with AMI.

Limitations

This study has several limitations. First, we had limited information on diabetes mellitus-related characteristics such as the duration, type, treatment, severity, or control of diabetes mellitus among young adults with AMI, restricting our ability to perform in-depth analyses on diabetes mellitus-related factors that could have modified each of the health status outcomes. For example, patients with newly diagnosed diabetes mellitus or with better glycemic control may have experienced relatively fewer clinical and social burdens of the disease (eg, taking more medication, checking glucose daily, suffering from diabetic complications) than those who had a longer duration or poorly controlled diabetes mellitus. The small sample size of patients with known diabetes mellitus type limits the generalization of results on the impact of diabetes mellitus type on health status. Future research focused on patients with diabetes mellitus should include more detailed assessments of diabetes mellitus characteristics and their influences on the association between diabetes mellitus and post-AMI health status outcomes. Second, a small proportion of our patients with diabetes mellitus were identified through a single HbA1c test result, and this may not be sufficient to diagnose diabetes mellitus. In clinical practice, a repeated HbA1c test on a different day is required to confirm the diagnosis. Third, VIRGO is a longitudinal study, and some subjects (with and without diabetes mellitus) were lost to follow-up at 1 and 12 months. If those who did not participate in the follow-up were in poorer health than those included in the analysis, this could lead to biased estimation of the impact of diabetes mellitus on health status. However, our data showed that the rates of loss to follow-up were comparable between young AMI patients with and without diabetes mellitus. In addition, prior VIRGO analysis indicated that the differences in baseline characteristics between those lost to follow-up and those who participated were minor.[20] Fourth, we assessed health status outcomes at only 3 time points (baseline, 1 month, and 12 months). Collecting repeated measures of health status at more time points, for a more extended period, and at equal time intervals could increase the precision of describing changes in the recovery trajectory.

Conclusions

In VIRGO, young adults with diabetes mellitus, regardless of sex, had worse disease-specific health status and poorer general physical and mental functioning before AMI, as well as an inferior general quality of life during AMI hospitalization, which might have put them at greater risk for poor recovery after AMI. However, our data suggest that their health status recovery was rapid and robust following discharge, and by 1-year post-AMI, most of their health status outcomes were similar to patients without diabetes mellitus. Maybe young adults with diabetes mellitus are resilient, or are more responsive to the high-intensity care that is common post-AMI. More research is needed to explore what aspects of post-AMI care facilitate recovery and improve health status in the sub-group of AMI

patients with diabetes mellitus. Moreover, our results support the notion that current guideline management is probably equally effective in AMI patients with and without diabetes mellitus, and thus increasing the use of healthcare services may lead to improved symptoms, function, and quality of life in patients with diabetes mellitus.

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SUPPLEMENTAL MATERIAL

Table S1. Comparison of Clinical Outcomes between AMI Patients with and without Diabetes.

Clinical Outcomes	With Diabetes (N=1493, 42.64%)	Without Diabetes (N=2008, 57.36%)	P-Value*
In-Hospital Complications			
Re-infarction	15 (18.29%)	28 (25.45%)	0.2396
Heart failure	133 (9.01%)	109 (5.48%)	**<0.0001**
Cardiac arrhythmias	97 (6.55%)	151 (7.56%)	0.2510
Stroke/Transient ischemic attack	6 (0.40%)	6 (0.30%)	0.6029
Hemorrhagic complications	118 (7.94%)	153 (7.64%)	0.7447
Mortality			
In-hospital mortality	3 (0.20%)	1 (0.05%)	0.3189
30-day mortality	9 (0.60%)	12 (0.60%)	0.9891
1-year mortality	40 (2.72%)	32 (1.63%)	**0.0278**

*P-value testing whether the differences between patients with and without diabetes are statistically significant

Table S2. Comparison of Health Status between AMI Patients with Type 1 and Type 2 Diabetes.

Health Status	Type 1 Diabetes (N=104)	Type 2 Diabetes (N=742)	All Diabetes (N=1493)	P-Value (Type 1 vs. Type 2)*
Baseline				
SAQ-Angina Frequency	77.02 (26.47)	78.99 (23.88)	81.43 (22.17)	0.437
SAQ-Physical Limitation	72.57 (29.11)	73.41 (28.86)	76.76 (27.79)	0.786
SAQ-Quality of Life	51.01 (25.63)	52.52 (25.36)	55.34 (25.48)	0.572
SF-12 Mental Functioning	43.93 (11.90)	42.86 (12.93)	44.10 (12.65)	0.429
SF-12 Physical Functioning	38.14 (13.05)	39.65 (11.86)	41.25 (12.17)	0.234
EQ-5D-VAS	52.61 (23.09)	58.76 (22.45)	61.39 (22.25)	**0.0011**
1-Month				
SAQ-Angina Frequency	84.00 (19.65)	87.78 (18.08)	88.09 (18.33)	0.065
SAQ-Physical Limitation	83.88 (24.17)	89.62 (20.31)	89.62 (20.13)	**0.0398**
SAQ-Quality of Life	57.77 (26.08)	67.51 (25.95)	68.13 (25.81)	**0.0009**
SF-12 Mental Functioning	46.57 (12.21)	48.64 (11.30)	49.67 (10.72)	0.123
SF-12 Physical Functioning	35.83 (13.68)	38.03 (11.36)	39.52 (11.91)	0.166
EQ-5D-VAS	63.79 (23.01)	67.22 (22.41)	69.04 (21.65)	0.177
12-Month				
SAQ-Angina Frequency	88.23 (20.24)	88.94 (19.40)	90.43 (17.60)	0.7606
SAQ-Physical Limitation	88.36 (20.26)	90.19 (21.58)	91.11 (19.78)	0.2982
SAQ-Quality of Life	64.50 (26.05)	70.09 (25.28)	72.33 (24.00)	0.074
SF-12 Mental Functioning	47.17 (12.39)	48.94 (11.76)	49.72 (11.12)	0.230
SF-12 Physical Functioning	39.98 (12.59)	40.20 (12.83)	42.24 (12.78)	0.889
EQ-5D-VAS	65.12 (22.79)	68.41 (22.74)	71.23 (21.57)	0.247

*P-value testing whether the differences between patients with type 1 and type 2 diabetes are statistically significant

Table S3. Associations between Diabetes and (A) SAQ-Angina Frequency Scores, (B) SAQ-Physical Limitation Scores, (C) SAQ-Quality of Life Scores, (D) SF-12 Mental Composite Summary, (E) SF-12 Physical Composite Summary, (F) EQ-VAS EuroQol-Visual Analogue Scales after AMI by Linear Mixed Effects Models.

(A) SAQ-Angina Frequency	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-2.68	-3.61	-1.76	<0.0001
Adjusted #1: Unadjusted model + Time				
Diabetes	-2.64	-3.56	-1.72	<0.0001
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-2.35	-3.27	-1.43	<0.0001
Adjusted #2 + Diabetes, Time, and Sex Interactions				
Diabetes-sex interaction				0.1593
Diabetes-time interaction				<0.0001
Sex-time interaction				0.5747
Adjusted #3: Adjusted #2 + Diabetes-time interaction + Other socio-demographics				
Diabetes time1	-3.23	-4.76	-1.69	<0.0001
Diabetes time3	-0.34	-1.93	1.26	0.6780
Diabetes-time interaction				<0.0001
Adjusted #4: Adjusted #3 + Diabetes-time interaction + CVD risk factors				
Diabetes time1	-3.23	-4.76	-1.70	<0.0001
Diabetes time3	-0.33	-1.92	1.27	0.6874
Diabetes-time interaction				<0.0001
Adjusted #5: Adjusted #4 + Diabetes-time interaction + Other comorbidities				
Diabetes time1	-3.24	-4.77	-1.71	<0.0001
Diabetes time3	-0.41	-2.01	1.18	0.6100
Diabetes-time interaction				<0.0001
Adjusted #6: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics				
Diabetes time1	-3.25	-4.78	-2.49	<0.0001
Diabetes time3	-0.39	-1.99	1.19	0.6269
Diabetes-time interaction				<0.0001
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes time1	-3.25	-4.78	-1.72	<0.0001
Diabetes time3	-0.40	-1.99	1.20	0.6269
Diabetes-time interaction				<0.0001
Occlusion ≥50%	1.11	-0.08	2.29	0.0685
Adjusted #7: Adjusted #6 + Diabetes-time interaction + Psychosocial factors				
Diabetes time1	-3.26	-4.79	-1.73	<0.0001
Diabetes time3	-0.45	-2.04	1.14	0.5828
Diabetes-time interaction				<0.0001
Adjusted #8: Adjusted #7 + Diabetes-time interaction + Health care utilization				
Diabetes time1	-3.26	-4.49	-2.48	<0.0001

Diabetes time3	-0.45	-2.04	1.15	0.5834
Diabetes-time interaction				<0.0001
Adjusted #9 (final model): Adjusted #8 + Diabetes-time interaction + AMI treatment				
Diabetes time1	-3.26	-4.79	-1.73	<0.0001
Diabetes time3	-0.45	-2.04	1.14	0.5788
Diabetes-time interaction				<0.0001
Interaction between diabetes and sex: Adjusted #9 + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.1666
Exploratory Analysis: Adjusted #9 + Diabetes-time interaction + Type of Diabetes				
Diabetes time1	-3.26	-4.79	-1.73	<0.0001
Diabetes time3	-0.45	-2.05	1.14	0.5769
Diabetes (Type 1 vs. Type 2)	-2.21	-4.87	0.44	0.1026
Diabetes-time interaction				<0.0001
Interaction between diabetes and sex: Exploratory Analysis 2 + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.0900

(B) SAQ-Physical Limitation	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-3.14	-4.24	-2.03	<0.0001
Adjusted #1: Unadjusted model + time				
Diabetes	-3.05	-4.16	-1.96	<0.0001
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-2.58	-3.67	-1.49	<0.0001
Adjusted #2 + Diabetes, Time, and Sex Interactions				
Diabetes-sex interaction				0.2091
Diabetes-time interaction				<0.0001
Sex-time interaction				0.0008
Adjusted #3: Adjusted #2 + Diabetes-time interaction + Sex-time interaction + Other socio-demographics				
Diabetes time1	-7.03	-8.81	-5.25	<0.0001
Diabetes time3	-0.59	-2.44	1.27	0.5341
Diabetes-time interaction				<0.0001
Sex-time				0.0008
Adjusted #4: Adjusted #3 + Diabetes-time interaction + Sex-time interaction + CVD risk factors				
Diabetes time1	-7.03	-8.81	-5.25	<0.0001
Diabetes time3	-0.59	-2.44	1.26	0.5325
Diabetes-time interaction				<0.0001
Sex-time				0.0009
Adjusted #5: Adjusted #4 + Diabetes-time interaction + Sex-time interaction + Other comorbidities				

Diabetes time1	-7.05	-8.83	-5.27	<0.0001
Diabetes time3	-0.71	-2.57	1.14	0.4515
Diabetes-time interaction				<0.0001
Sex-time				0.0009
Adjusted #6: Adjusted #5 + Diabetes-time interaction + Sex-time interaction + AMI clinical characteristics				
Diabetes time1	-7.06	-8.84	-5.28	<0.0001
Diabetes time3	-0.68	-2.53	1.17	0.4717
Diabetes-time interaction				<0.0001
Sex-time				0.0009
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes time1	-7.17	-8.94	-5.39	<0.0001
Diabetes time3	-0.67	-2.53	1.18	0.4773
Diabetes-time interaction				<0.0001
Sex-time				0.0013
Occlusion ≥50%	1.47	-0.09	2.86	0.0361
Adjusted #7: Adjusted #6 + Diabetes-time interaction + Sex-time interaction + Psychosocial factors				
Diabetes time1	-7.06	-8.84	-5.28	<0.0001
Diabetes time3	-0.68	-2.53	1.17	0.4196
Diabetes-time interaction				<0.0001
Sex-time				0.0010
Adjusted #8: Adjusted #7 + Diabetes-time interaction + Sex-time interaction + Health care utilization				
Diabetes time1	-7.09	-8.86	-5.31	<0.0001
Diabetes time3	-0.75	-2.59	1.10	0.4273
Diabetes-time interaction				<0.0001
Sex-time				0.0010
Adjusted #9 (final model): Adjusted #8 + Sex-time interaction + Diabetes-time interaction + AMI treatment				
Diabetes time1	-7.19	-8.96	-5.41	<0.0001
Diabetes time3	-0.74	-2.59	1.10	0.4312
Diabetes-time interaction				<0.0001
Sex-time				0.0015
Interaction between diabetes and sex: Adjusted #9 + Sex-time interaction + Diabetes-time interaction + Sex-diabetes interaction				
Sex-diabetes				0.1782
Exploratory Analysis: Adjusted #9 + Sex-time interaction + Diabetes-time interaction + Type of Diabetes				
Diabetes time1	-7.18	-8.96	-5.40	<0.0001
Diabetes time3	-0.73	-2.59	1.12	0.4371
Diabetes (Type 1 vs. Type 2)	-2.13	-5.21	0.95	0.1745
Diabetes-time interaction				<0.0001
Sex-time				0.0015

Interaction between diabetes and sex: Exploratory Analysis + Sex-time interaction + Diabetes-time interaction + Sex-diabetes interaction				
Sex-diabetes				0.1657

(C) SAQ-Quality of Life	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-0.94	-2.25	0.35	0.1532
Adjusted #1: Unadjusted model + time				
Diabetes	-0.83	-2.13	0.47	0.2100
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-0.23	-1.51	1.05	0.7258
Adjusted #2 + Diabetes, Time, Sex Interactions				
Diabetes-sex interaction				0.4998
Diabetes-time interaction				0.0136
Sex-time interaction				0.1486
Adjusted #3: Adjusted #2 + Diabetes-time interaction + Other socio-demographics				
Diabetes time1	-2.47	-4.33	-0.61	0.0093
Diabetes time3	-0.14	-2.10	1.82	0.8873
Diabetes-time interaction				0.0197
Adjusted #4: Adjusted #3 + Diabetes-time interaction + CVD risk factors				
Diabetes time1	-2.48	-4.34	-0.62	0.0089
Diabetes time3	-0.15	-2.12	1.81	0.8739
Diabetes-time interaction				0.0194
Adjusted #5: Adjusted #4 + Diabetes-time interaction + Other comorbidities				
Diabetes time1	-2.49	-4.35	-0.62	0.0088
Diabetes time3	-0.25	-2.21	1.71	0.8034
Diabetes-time interaction				0.0209
Adjusted #6: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics				
Diabetes time1	-2.48	-4.34	-0.63	0.0088
Diabetes time3	-0.21	-2.17	1.76	0.8357
Diabetes-time interaction				0.0201
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes time1	-2,49	-4.35	-0.63	0.6269
Diabetes time3	-0.21	-2.17	1.75	0.8311
Diabetes-time interaction				0.0201
Occlusion ≥50%	0.18	3.47	2.29	0.0293
Adjusted #7: Adjusted #6 + Diabetes-time interaction + Psychosocial factors				
Diabetes time1	-2.51	-4.37	-0.65	0.0081
Diabetes time3	-0.27	-2.23	1.69	0.7889
Diabetes-time interaction				0.0198
Adjusted #8: Adjusted #7 + Diabetes-time interaction + Health care utilization				
Diabetes time1	-2.51	-4.37	-0.65	0.0082
Diabetes time3	-0.27	-2.23	1.69	0.7866

Diabetes-time interaction				0.0201
Adjusted #9 (final model): Adjusted #8 + Diabetes-time interaction + AMI treatment				
Diabetes time1	-2.51	-4.37	-0.65	<0.0001
Diabetes time3	-0.29	-2.25	1.67	0.7704
Diabetes-time interaction				0.0204
Interaction between diabetes and sex: Adjusted #9 + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.6086
Exploratory Analysis: Adjusted #9 + Diabetes-time interaction + Type of Diabetes				
Diabetes time1	-2.50	-4.36	-0.64	<0.0001
Diabetes time3	-0.29	-2.26	1.66	0.7648
Diabetes (Type 1 vs. Type 2)	-4.41	-7.95	-0.88	0.0142
Diabetes-time interaction				0.0144
Interaction between diabetes and sex: Exploratory Analysis + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.3717

(D) SF-12 Mental Functioning	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-1.09	-1.73	-0.44	0.0009
Adjusted #1: Unadjusted model + time				
Diabetes	-1.05	-1.69	-0.41	0.0013
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-0.69	-1.32	-0.07	0.0305
Adjusted #2 + Diabetes, Time, and Sex Interactions				
Diabetes-sex interaction				0.1292
Diabetes-time interaction				<0.0001
Sex-time interaction				0.2026
Adjusted #3: Adjusted #2 + Diabetes-time interaction + Other socio-demographics				
Diabetes time1	-2.11	-2.99	-1.23	<0.0001
Diabetes time3	-0.91	-1.83	0.003	0.05
Diabetes-time interaction				<0.0001
Adjusted #4: Adjusted #3 + Diabetes-time interaction + CVD risk factors				
Diabetes time1	-2.12	-3.00	-1.24	<0.0001
Diabetes time3	-0.92	-1.83	0.002	0.05
Diabetes-time interaction				<0.0001
Adjusted #5: Adjusted #4 + Diabetes-time interaction + Other comorbidities				
Diabetes time1	-2.08	-2.95	-1.20	<0.0001
Diabetes time3	-0.94	-1.86	-0.02	0.04
Diabetes-time interaction				<0.0001
Adjusted #6: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics				
Diabetes time1	-2.08	-2.96	-1.20	<0.0001
Diabetes time3	-0.93	-1.84	-0.01	0.05

Diabetes-time interaction				<0.0001
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes time1	-2.08	-2.95	-1.20	<0.0001
Diabetes time3	-0.93	-1.84	-0.01	0.6269
Diabetes-time interaction				<0.0001
Occlusion ≥50%	0.38	-0.41	1.18	0.0685
Adjusted #7: Adjusted #6 + Diabetes-time interaction + Psychosocial factors				
Diabetes time1	-2.07	-2.94	-1.20	<0.0001
Diabetes time3	-0.93	-1.84	-0.02	0.05
Diabetes-time interaction				<0.0001
Adjusted #8: Adjusted #7 + Diabetes-time interaction + Health care utilization				
Diabetes time1	-2.06	-2.94	-1.19	<0.0001
Diabetes time3	-0.93	-1.83	-0.02	0.05
Diabetes-time interaction				<0.0001
Adjusted #9: Adjusted #8 + Diabetes-time interaction + AMI treatment				
Diabetes time1	-2.07	-2.94	-1.20	<0.0001
Diabetes time3	-0.93	-1.84	-0.03	0.0433
Diabetes-time interaction				<0.0001
Interaction between diabetes and sex: Adjusted #9 + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.1202
Exploratory Analysis: Adjusted #9 + Diabetes-time interaction + Type of Diabetes				
Diabetes time1	-2.06	-2.93	-1.19	<0.0001
Diabetes time3	-0.93	-1.84	-0.03	0.0421
Diabetes (Type 1 vs. Type 2)	-0.60	-2.06	0.86	0.4217
Diabetes-time interaction				<0.0001
Interaction between diabetes and sex: Exploratory Analysis + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.0861

(E) SF-12 Physical Functioning	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-4.23	-4.91	-3.54	<0.0001
Adjusted #1: Unadjusted model + Time				
Diabetes	-4.21	-4.90	-3.52	<0.0001
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-3.48	-4.20	-2.76	<0.0001
Adjusted #2 + Diabetes, Time, and Sex Interactions				
Diabetes-sex interaction				0.5123
Diabetes-time interaction				0.2283
Sex-time interaction				0.1283
Adjusted #3: Adjusted #2 + Other socio-demographics				

Diabetes	-2.49	-3.11	-1.86	<0.0001
Adjusted #4: Adjusted #3 + CVD risk factors				
Diabetes	-1.65	-2.30	-1.09	<0.0001
Adjusted #5: Adjusted #4 + Other comorbidities				
Diabetes	-1.28	-1.92	-0.66	<0.0001
Adjusted #6: Adjusted #5 + AMI clinical characteristics				
Diabetes	-1.04	-1.67	-0.41	0.0013
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes	-1.01	-1.65	-0.38	0.0018
Occlusion ≥50%	0.46	-0.33	1.28	0.2499
Adjusted #7: Adjusted #6 + Psychosocial factors				
Diabetes	-0.85	-1.47	-0.23	0.0070
Adjusted #8: Adjusted #7 + Health care utilization				
Diabetes	-0.75	-1.37	-0.14	0.0168
Adjusted #9 (final model): Adjusted #8 + AMI treatment				
Diabetes	-0.67	-1.29	-0.05	0.0344
Interaction between diabetes and time: Adjusted #9 + Diabetes-time interaction				
Diabetes-time interaction				0.3101
Interaction between diabetes and sex: Adjusted #9 + Diabetes-sex interaction				
Sex-Diabetes				0.8421
Exploratory Analysis: Adjusted #9 + Type of Diabetes				
Diabetes	-0.28	-1.03	0.47	0.4641
Diabetes (Type 1 vs. Type 2)	-1.24	-3.02	0.53	0.1681
Interaction between diabetes and time: Exploratory Analysis + Diabetes-time interaction				
Diabetes-time interaction				0.3173
Interaction between diabetes and sex: Exploratory Analysis + Diabetes-sex interaction				
Sex-Diabetes				0.8421

(F) EQ-VAS	Parameter Estimates	95% CI Lower	95% CI Upper	P-value
Unadjusted model: Diabetes alone and random effect of intercept among patients				
Diabetes	-3.54	-4.69	-2.39	<0.0001
Adjusted #1: Unadjusted model + Time				
Diabetes	-3.49	-4.64	-2.34	<0.0001
Adjusted #2: Adjusted #1 + Sex				
Diabetes	-3.13	-4.27	-1.98	<0.0001
Adjusted #2 + Diabetes, Time, and Sex Interactions				
Diabetes-sex interaction				0.8554
Diabetes-time interaction				0.0051
Sex-time interaction				0.1238
Adjusted #3: Adjusted #2 + Diabetes-time interaction + Other socio-demographics				
Diabetes time1	-2.14	-3.72	-0.56	0.0080
Diabetes time3	0.39	-1.27	2.05	0.64

Diabetes-time interaction				0.0086
Adjusted #4: Adjusted #3 + Diabetes-time interaction + CVD risk factors				
Diabetes time1	-2.14	-3.71	-0.56	0.0080
Diabetes time3	0.38	-1.27	2.04	0.65
Diabetes-time interaction				0.0088
Adjusted #5: Adjusted #4 + Diabetes-time interaction + Other comorbidities				
Diabetes time1	-2.14	-3.72	-0.56	0.0079
Diabetes time3	0.27	-1.38	1.92	0.74
Diabetes-time interaction				0.0106
Adjusted #6: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics				
Diabetes time1	-2.15	-3.73	-0.57	0.0077
Diabetes time3	0.29	-1.36	1.94	0.73
Diabetes-time interaction				0.0101
Adjusted #6 v2: Adjusted #5 + Diabetes-time interaction + AMI clinical characteristics (including coronary occlusion ≥50%)				
Diabetes time1	-2.15	-3.73	-0.56	0.0078
Diabetes time3	0.29	-1.37	1.94	0.6269
Diabetes-time interaction				0.0101
Occlusion ≥50%	0.51	-0.95	1.99	0.0493
Adjusted #7: Adjusted #6 + Diabetes-time interaction + Psychosocial factors				
Diabetes time1	-2.17	-3.75	-0.59	0.0072
Diabetes time3	0.26	-1.40	1.91	0.76
Diabetes-time interaction				0.0099
Adjusted #8: Adjusted #7 + Diabetes-time interaction + Health care utilization				
Diabetes time1	-2.16	-3.74	-0.58	0.0074
Diabetes time3	0.26	-1.39	1.91	0.75
Diabetes-time interaction				0.0101
Adjusted #9 (final model): Adjusted #8 + Diabetes-time interaction + AMI treatment				
Diabetes time1	-2.16	-3.74	-0.58	0.0074
Diabetes time3	0.09	-1.56	1.75	0.9083
Diabetes-time interaction				0.0113
Interaction between diabetes and sex: Adjusted #9 + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.6892
Exploratory Analysis: Adjusted #9 + Diabetes-time interaction + Type of Diabetes				
Diabetes time1	-2.15	-3.73	-0.57	0.0076
Diabetes time3	0.23	-1.42	1.89	0.7812
Diabetes (Type 1 vs. Type 2)	-4.16	-7.34	-0.95	0.0106
Diabetes-time interaction				0.0109
Interaction between diabetes and sex: Exploratory Analysis + Diabetes-time interaction + Diabetes-sex interaction				
Sex-diabetes				0.9136

Other socio-demographics: Age, race, Hispanic (yes/no), marital status, education status, employment status, and household income

CVD risk factors: family history of CVD, hypertension, hypercholesterolemia, smoking in the past 30 days, sleep apnea, body mass index ≥30 kg/m^2
Other comorbidities: renal dysfunction, heart failure, stroke/TIA, depression, history of alcohol abuse, prior MI, prior PCI
AMI clinical characteristics: AMI symptom presentation, ST-elevation MI, initial systolic BP, initial diastolic BP, initial HR, peak troponin, ejection fraction <40%, time to presentation >6hrs, GRACE scores
Psychosocial factors: baseline social support, baseline stress, baseline depressive symptom score
Health care utilization: health insurance (yes/no), difficulty in obtaining medical care, medical costs have been an economic burden over the past year, avoided health care because of cost, frequently not taken a medication because of cost
AMI treatment: Coronary revascularization (PCI/CABG), diagnostic angiography, aspirin at arrival, reperfusion therapy (fibrinolytic therapy and primary angioplasty), discharge medication: aspirin, statin, beta-blocker, ACEI or ARB
CABG=coronary artery bypass grafting; CVD=cardiovascular disease; MI=myocardial infarction; PCI=percutaneous coronary intervention; GRACE=Global Registry of Acute Coronary Events (higher scores indicating higher risk of death); SAQ=Seattle Angina Questionnaire; SF-12=12-Item Short Form Health Survey; EQ-VAS=EuroQol-Visual Analogue Scales; Time1=Baseline; Time2=1-month follow-up; Time3=12-month follow-up

Figure S1. Flowchart Illustrating the Follow-up of AMI Patients, Stratified by Diabetes Status and by Sex.