Patterns and Predictors of Intensive Statin Therapy Among Patients With Diabetes Mellitus After Acute Myocardial Infarction

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Intensive statin therapy is a central component of secondary prevention after acute myocardial infarction (AMI), particularly among high-risk patients, such as those with diabetes mellitus (DM). However, the frequency and predictors of intensive statin therapy use after AMI among patients with DM have not been described. We examined patterns of intensive statin therapy use (defined as a statin with expected low-density lipoprotein cholesterol lowering of >50%) at discharge among patients with AMI with known DM enrolled in a 24-site US registry. Predictors of intensive statin therapy use were evaluated using multivariable hierarchical Poisson regression models. Among 1,300 patients with DM after AMI, 22% were prescribed intensive statin therapy at hospital discharge. In multivariable models, ST-elevation AMI (risk ratio [RR] 1.48, 95% confidence interval [CI] 1.29 to 1.70), insurance for medications (RR 1.28, 95% CI 1.00 to 1.63), and higher low-density lipoprotein cholesterol levels (RR 1.05 per 1 mg/dl, 95% CI 1.02 to 1.07) were independent predictors of intensive statin therapy, whereas higher Global Registry of Acute Coronary Events scores were associated with lower rates of intensive statin therapy (RR 0.94 per 10 points, 95% CI 0.91 to 0.98). In conclusion, only 1 in 5 patients with DM was prescribed intensive statin therapy at discharge after an AMI. Predictors of intensive statin therapy use suggest important opportunities to improve quality of care in this patient population. **(Am J Cardiol 2014;113:1267−1272)**

Patients with diabetes mellitus (DM) experience higher rates of mortality and recurrent events after acute myocardial infarction (AMI) than those without DM.[1−4] Aggressive secondary prevention strategies are, therefore, critical in this patient population and supported by contemporary practice guidelines.[5] A key component of secondary prevention after AMI is intensive statin therapy that has been shown to be superior to moderate statin treatment in reducing morbidity and mortality after AMI.[6−10] Despite these data, recent analyses from the United States reveal that only ∼38% of patients with AMI are discharged on intensive statin therapy.[11] Patients with DM represent one of the highest risk subgroups of patients with AMI and thus have the most potential to benefit from aggressive secondary prevention efforts; however, the frequency and predictors of intensive statin therapy among patients with DM are unknown. Addressing this knowledge gap could identify an important opportunity for quality improvement efforts to support aggressive treatment in those most likely to benefit.

Methods

Details of the Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) study, including the study design, patient selection, site characteristics, informed consent, appropriate treatment of research subjects, and follow-up assessments, have been previously published.[12] From April 2005 to December 2008, patients from 24 US hospitals were enrolled into the TRIUMPH registry. Patients were required to have biomarker evidence of myocardial necrosis and additional clinical evidence supporting the diagnosis of an AMI, such as prolonged ischemic signs/symptoms (≥20 minutes) or electrocardiographic ST changes during the initial 24 hours of admission. For this analysis, only patients with established DM were included, which was defined as a chart-documented history of DM or taking any glucose-lowering medication on admission.

Baseline sociodemographic and clinical data were obtained through chart abstraction and a detailed structured interview within 24 to 72 hours of admission. Lipid-lowering medications (type and dose) were documented at admission and hospital discharge. Statins prescribed at discharge were categorized as intensive (expected low-density lipoprotein cholesterol [LDL-C] lowering of >50%[13]; i.e., atorvastatin 80 mg or rosuvastatin ≥20 mg daily)[11] or moderate (all other statins). As a sensitivity analysis, given the new cholesterol guidelines,[14] we also considered atorvastatin 40 mg as

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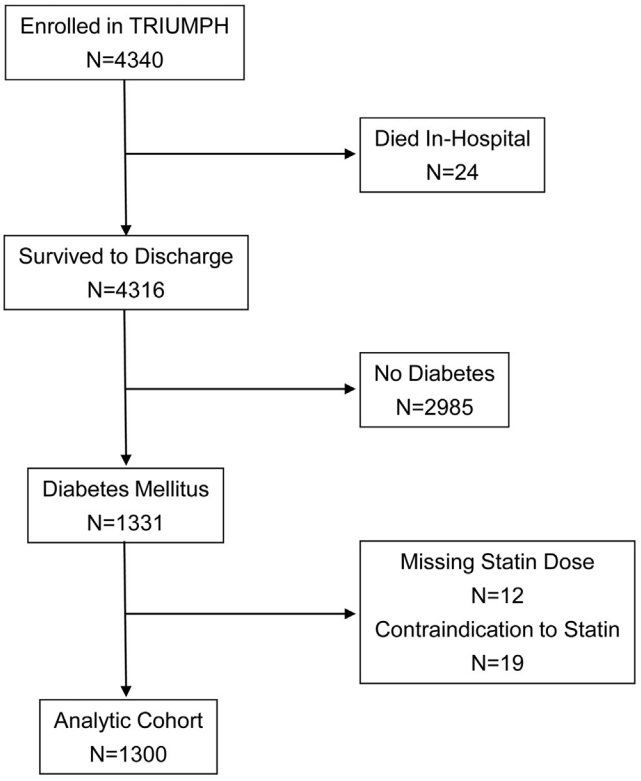

Figure 1. Flowchart of analytic cohort.

intensive statin therapy (estimated LDL-C lowering of 45% to 50%). In addition, as a second sensitivity analysis, to account for hospitals with restrictive formularies, we excluded the 4 hospitals with limited access to intensive statins. Patients with documented allergies or contraindications to statin therapy were excluded from the analysis. Institutional review board approval was obtained at each participating hospital, and informed consent was obtained from all patients for baseline and follow-up assessments.

The demographic and clinical characteristics of patients with DM who did and who did not receive intensive statin therapy at discharge after AMI were compared using chi-square test for categorical variables and *t* test for continuous variables. We used hierarchical modified Poisson regression with robust standard errors to examine the factors associated with prescription of intensive statin therapy at hospital discharge because our primary metric of interest (frequency of intensive statin prescription) was not rare, to avoid an overestimation of effect sizes, as could result from using logistic regression. Covariates included in the multivariable model were selected a priori based on clinical judgment and included sociodemographics (age, sex, race, marital status, and prescription drug insurance), clinical features (history of smoking and body mass index), characteristics of the qualifying AMI event (ST-elevation myocardial infarction [STEMI] and Global Registry of Acute Coronary Events [GRACE] score—an assessment of the severity of AMI where higher scores indicate a higher risk of mortality[15]), severity of DM (duration of DM, class of DM therapy [diet vs oral medications only vs any insulin therapy]), HbA1c level $\geq$7%, and LDL-C level. Participating center was entered as a random effect to account for clustering of patients within hospitals. Site variability in the rates of intensive statin therapy was evaluated using median rate ratios, which estimates the relative difference in risk ratios of 2 hypothetically identical patients for being discharged on intensive statin therapy at 2 different sites. All analyses were conducted using SAS v9.2 (SAS Institute, Inc., Cary, North Carolina), and statistical significance was determined by a 2-sided p value of <0.05.

Results

Of the 4,340 patients enrolled in TRIUMPH, 4,316 survived to hospital discharge, of whom 1,331 (31%) had an established diagnosis of DM at admission. Statin dose was not available for 12 patients with DM, and 19 had a documented contraindication to statins, which resulted in an analytic population of 1,300 patients (Figure 1). The mean age of the population was 61 years, 59% were men, and 58% were Caucasian (Table 1). About 1/3 of patients presented with an STEMI, and 66% underwent invasive management of their AMI. The mean duration of DM was 12 years, mean HbA1c was 8.3%, and 32% were on insulin at admission (Table 2).

Among the 1,300 patients with DM who were hospitalized with an AMI, 1,138 (88%) were discharged on a statin at any dose, but only 280 (22%) were prescribed intensive statin therapy. In sensitivity analyses, when 40 mg of atorvastatin was considered intensive statin therapy, and additional 117 (9%) of patients were considered as receiving intensive statins, for an overall rate of intensive statin prescription of 31%. In a second sensitivity analysis, when the 4 sites with restrictive formularies were excluded from the analysis, the overall rate of intensive statin prescription was 26%.

Compared with those not discharged on intensive statins, patients with DM discharged on intensive statin therapy were more likely to have prescription medication insurance coverage, less often had a history of congestive heart failure, and were more likely to have presented with an STEMI (Table 1). Patients discharged on intensive statin therapy had higher HbA1c levels and higher LDL-C levels (Table 2), although DM duration and glucose-lowering treatments were similar between groups.

In the hierarchical, multivariable model, patients who presented with an STEMI were 48% more likely to be discharged on intensive statin therapy (95% confidence interval 1.29 to 1.70; Figure 2). Other factors independently associated with a higher rate of intensive statin therapy at discharge were insurance for prescription medications and higher LDL-C levels. Paradoxically, higher GRACE scores were associated with a lower rate of intensive statin therapy. None of the DM severity measures were significantly associated with frequency of discharge prescription of intensive statin therapy, including DM duration, insulin treatment, or HbA1c level $\geq$7%.

Among the 24 hospitals in TRIUMPH, the unadjusted rates of intensive statin therapy at discharge ranged from 0% to 67%, with a median rate of 14% (Figure 3). In the hierarchical multivariable model that adjusted for patient factors, the median rate ratio was 2.18 (95% confidence interval 1.75 to 3.61), indicating that 2 identical patients had more than twofold difference in the likelihood of being discharged