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Factors Predicting Beta-Blocker Treatment after Myocardial Infarction in Patients with Type 2 Diabetes

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OBJECTIVE – Beta-blockers remain important for secondary prevention after myocardial infarction (MI). Despite clinical guideline recommendations, the potential for poor glycemic control and masking warning signs of hypoglycemia limit their utilization in type 2 diabetes. This study evaluated factors predicting post-MI beta-blocker initiation among type 2 diabetic patients.

RESEARCH DESIGN AND METHODS – A retrospective cohort of employed, commercially insured individuals was developed using de-identified enrollment files, medical claims, and pharmacy claims from 2007-2009 in the U.S. Inclusion criteria: (1) type 2 diabetes, (2) ≥18 years old, (3) continuous eligibility, (4) MI. Exclusion criteria: (1) females prescribed metformin exclusively without diabetes diagnosis, (2) <6 months eligibility pre-MI, (3) MI before diabetes identified, (4) pre-MI beta-blocker, (5) receipt of sotalol post-MI, (6) no prescription claims, (7) <30 days between discharge and study end. Multivariable logistic regression with manual backward elimination was used to evaluate predictors of beta-blocker initiation.

RESULTS – Of 341 type 2 diabetic patients, only 167 (49.0%) initiated beta-blockers within 30 days of discharge. Patients on a calcium channel blocker (OR_{adj}: 2.63) and patients taking 1 to 5 medications (OR_{adj}: 3.59) were more likely to initiate beta-blockers post-MI. Patients with heart failure (OR_{adj}: 0.45) or an arrhythmia (OR_{adj}: 0.44) were less likely to initiate beta-blockers as well as patients with renal failure who are not taking a diuretic (OR_{adj}: 0.17).

CONCLUSIONS – Although these results might not apply to older populations, they support the need for further investigation to determine whether more patients with type 2 diabetes could benefit from beta-blocker treatment post-MI.

Existing evidence on the effect of beta-blockers in decreasing myocardial ischemia, re-infarction, and the frequency of complex ventricular dysrhythmias as well as increasing long-term survival supports the key role these drugs play in secondary prevention after myocardial infarction (MI).[1] In fact, current guidelines for cardiovascular secondary prevention recommend initiation of oral beta-blockers within 24 hours of a MI;[1,2] furthermore, in patients with an ST-elevation MI (STEMI), this therapy is recommended for 3 years post-MI.[2]

However, beta-blockers have a history of relative contraindication in diabetic patients based on their potential to mask the warning signs of hypoglycemia[3-7] and negatively impact glycemic control through beta-3 adrenergic receptor blockade on adipocytes.[5,7-10] These effects are potentially more likely for nonselective beta-blockers. This brings about somewhat of a paradox. Patients with type 2 diabetes typically have worse cardiovascular outcomes after MI,[7] suggesting they may have more to gain from beta-blocker therapy for secondary prevention. However, cardiovascular outcomes in diabetic patients are often improved through tight glycemic control,[9] which may be worsened by beta-blocker therapy. There is also evidence that beta-blockers restore sympathovagal balance in diabetic patients with neuropathy and may also decrease the use of fatty acids in the myocardium, thereby decreasing oxygen demand.[4]

Although current guidelines from the American Diabetes Association (ADA) recommend the use of beta-blockers in type 2 diabetic patients after a MI,[11,12] few studies have formally evaluated the use of beta-blockers in this population.[3,13-17] One observational study from Canada in the 1990s found that approximately 43% of type 2 diabetic patients without previous exposure received beta-blockers after a MI.[3] Other

studies have also found low rates of beta-blocker utilization among patients with type 2 diabetes when compared to patients without diabetes.[14,15] Patients taking other medications with an elevated risk of hypoglycemia (e.g. insulin and sulfonylureas) may be even less likely to be prescribed beta-blockers after a MI.[15]

Few studies have evaluated beta-blocker utilization among patients with type 2 diabetes after a MI in the United States.[15,16] While clinical guidelines are relatively straightforward in this population, it is important to understand why real-world practice deviates from these recommendations so often. The purpose of this study was to determine the clinical and socioeconomic characteristics of type 2 diabetic patients that predict initiation of a beta-blocker to identify which patients are more or less likely to receive beta-blockers after MI. These predictors would provide useful knowledge of potential confounders to include in the evaluation of outcomes related to beta-blocker therapy. Also, clinicians and policymakers could potentially utilize this information to help develop interventions to improve the rate beta-blocker initiation in a post-MI setting if the treatment benefits are indeed significant for type 2 diabetic patients.

Research Design and Methods

Settings and databases

This study was conducted using secondary claims data from a population of employed, commercially insured individuals with dependents from January 2007 through December 2009. From this data, a retrospective cohort was developed to evaluate predictors of new users of beta-blockers among type 2 diabetic patients after discharge

from hospitalization due to MI. The de-identified dataset included information on patient enrollment files, medical claims, and pharmacy claims.

The following inclusion criteria were used to identify patients with type 2 diabetes post-MI: (1) diabetes identified through the first instance of ICD-9 codes for type 2 diabetes in medical claims or prescription claims for oral diabetes medications identified through National Drug Codes (NDCs), (2) patients who were at least 18 years of age, (3) continuous eligibility through the entire study period, and (4) MI identified through ICD-9 codes (all codes of the form 410.X1 as the primary or secondary diagnosis only). If a patient had multiple MIs during the study period, the first episode was considered the index MI.

Exclusion criteria included the following: (1) females with no type 2 diabetes diagnosis and receiving metformin as the exclusive oral diabetes medication, (2) less than 6 months of eligibility prior to first MI identified, (3) MI identified in claims before diabetes was identified, (4) receipt of a beta-blocker in prescription claims in the 6 months prior to index MI, (5) receipt of sotalol as the first beta-blocker after MI, (6) no prescription claims for the duration of the study, and (7) less than 30 days between index discharge date and the end of the study. Female patients having no ICD-9 diagnosis for diabetes and receiving only metformin were excluded to prevent misclassification of patients with polycystic ovary syndrome as patients with diabetes. Patients receiving the beta-blocker sotalol after MI were excluded as this medication is indicated for the treatment of arrhythmias and is not indicated for secondary prevention of MI. See Figure 1 for a flowchart depicting study design and cohort selection.

Predictors of beta-blocker initiation

Predictors of beta-blocker receipt were demographic and clinical characteristics as well as measures of health care utilization. Demographic characteristics investigated include age, sex, race, and proxy measures of socioeconomic status including education, annual household income, and geographic region of residence. Clinical characteristics included both comorbidities and other medications the patient was taking prior to MI. Comorbidities were identified through the Elixhauser Comorbidity algorithm for the 6 months preceding MI[18] (see Table 1 for a full list of comorbidities). Patients taking insulin or insulin secretagogues (sulfonylureas and meglitinides) 90 days before index MI were identified, as these patients are likely at a higher risk of hypoglycemia. Additionally, patients taking any diabetes medication including insulin 90 days prior to index MI were identified. Patients taking other medications that could lower blood pressure were identified (see Table 1 for a full list of antihypertensive medication classes). Statin users were also identified to see if patients already taking post-MI recommended therapy were more likely to initiate beta-blockers.

Number of prescription medications filled in the 90 days before index MI was used as a measure of health care utilization. The American Hospital Formulary Service (AHFS) Drug Information code was used to identify unique classes of medication. NDCs are linked to the AHFS codes to group unique drug products into drug classes. Prescription claims with no AHFS code or that were coded as unknown were not included in this count. Additionally, AHFS codes for medical products such as glucagon emergency kits (682212), lancets and other insulin testing sharps (940000), and insulin testing strips (362600) were not included in this count. All other unique AHFS codes

were included in the number of prescription medications received in the 90 days before index MI. Additionally, patients with a prescription fill for insulin testing strips 90 days prior to MI were identified as patients who were currently testing their blood glucose. Some clinicians have stated that diabetic patients who self-monitor blood glucose may be better candidates for beta-blocker therapy after MI.[7]

Outcome

The primary outcome of interest was receipt of a beta-blocker as identified in prescription claims within 30 days after hospital discharge. Beta-blockers were identified using the AHFS code 242400; this includes all beta-blockers and all combination medications with a beta-blocker in it. Patients who initiated beta-blockers within 30 days of hospital discharge were considered new users of beta-blockers. All other patients were identified as non-users. As stated previously, patients with previous beta-blocker exposure greater than 6 months before index MI were kept in the cohort to prevent selection bias; these patients were defined as new users versus non-users based solely on having a prescription claim for a beta-blocker after index hospital discharge.

Statistical analysis

Baseline demographic, clinical, and health care utilization characteristics were summarized for the entire population. Age was the only continuous variable and was evaluated using mean ± standard deviation (SD). Categorical variables were summarized using number (%) of patients with the given characteristic.

Unadjusted bivariable statistics were used to compare new users to non-users of beta-blockers after MI among type 2 diabetic patients. A 2-sample t-test was used to compare the age of new users and non-users. For all other variables, a chi-square test (or

Fisher's exact test where appropriate) was used to compare new users to non-users (α = 0.05 for all bivariable analyses).

Descriptive statistics for the first prescription fill of beta-blockers among new users were also summarized including copay, beta-blocker agent used, and pharmacologic properties of beta-blocker used. Pharmacologic properties include cardioselective versus nonselective beta-blockers, beta-blockers with intrinsic sympathomimetic activity (ISA), and beta-blockers with auxiliary mechanisms of action such as alpha-antagonism and nitric oxide-dependent vasodilation.

A multivariable logistic regression model was utilized to predict new users and non-users of beta-blockers among type 2 diabetic patients after MI. The one patient (0.3%) with a missing value for race was added to the "Other" category, and missing values for education (N = 8; 2.3%) and income (N = 21; 6.2%) were replaced with the mode to allow patient inclusion in the regression analysis. Variables to be included in the initial regression model as predictors of receipt or non-receipt of beta-blockers were identified based on a combination of statistical significance in the bivariable analyses, identification in the literature, and clinical judgment (see Table 3 for a list of variables included in the initial model). Manual backward elimination was used to identify the best model using the Akaike information criterion (AIC) for model selection; variables with the highest *P* value were removed until the model with the minimum AIC value was identified. After model reduction, variables remaining in the model were evaluated for interactions using a similar manual backward elimination approach. Interactions to be included in the final model reduction were selected based on identification in the literature and clinical judgment. Adjusted odds ratios (OR_{adj}) with 95% confidence

intervals (CI) were reported for all variables included in the final model. Internal validation of the final predictive model was completed using leave-one-out cross-validation. All statistical analyses were completed using SAS® software (Version 9.4 of the SAS System for Windows, Copyright © 2002-2012, SAS Institute, Cary, NC).

Results

Description of study cohort

Out of 396,619 patients who were identified as having type 2 diabetes, 743 patients (about 1.9 out of 1,000 patients) had a MI during the 2007-2009 study period (Figure 1). Of these patients, 334 (45.0%) had a prescription claim for a beta-blocker within the 6 months before their index MI. After excluding patients with no prescription claims for the entire study period and patients discharged within 30 days of study end, 341 patients were included in the study cohort. Of these patients, 48 (14.1%) had previous exposure to a beta-blocker outside of the 6-month pre-MI window. When these patients were compared to the rest of the cohort, there was no significant difference in the rate of beta-blocker initiation after hospital discharge (unadjusted OR: 0.86; $P = 0.639$).

The mean age of the cohort was 63.3 years (Table 1). Most patients were white (76.2%) and 58.4% of patients were male. Only 64 patients (19.2% of those reporting) had received a college degree including an associate degree or higher. Self-reported annual household income was categorized based on the distribution of values in the cohort. Among patients who reported income, about half (54.1%) reported annual household incomes in the $30,000 to $74,999 range while 17.5% and 28.4% of patients

belonged to the lower and higher income brackets, respectively. A large proportion of patients (56.0%) resided in the South based on U.S. Census geographic regions.

The most common comorbidities identified among the cohort prior to the index MI (Table 1) were hypertension (66.9%), cardiac arrhythmia (21.7%), chronic pulmonary disease (21.4%), congestive heart failure (16.1%), and peripheral vascular disorder (15.0%). Polypharmacy was identified as having prescription claims for 6 or more AHFS classes of medications within 90 days prior to index MI; 156 (45.8%) of patients fell into this category while 62 (18.2%) and 123 (36.1%) patients had either no medications or 1 to 5 medications prior to MI, respectively. Only 165 (48.4%) had a prescription claim for a diabetes medication in the 90 days prior to index MI. Among these patients, 69 (20.2%) had a claim for insulin and 63 (18.5%) had a claim for either a sulfonylurea or a meglitinide. Only 67 (19.7%) of all cohort patients had an identified claim for blood glucose testing strips. The most common antihypertensive medications were ACE inhibitors and ARBs (111 patients; 32.6%) and diuretics (77 patients; 22.6%). Only 31 patients (9.1%) were on a calcium channel blocker. There were 130 patients (38.1%) who received a statin in the 90 days prior to MI. Among the final cohort, 167 patients (49.0%) were identified as new users of beta-blockers while 174 patients (51.0%) were identified as non-users.

Bivariable analyses

New users (61.1 ± 11.1) were younger than non-users (65.3 ± 14.5; $P = 0.003$) of beta-blockers post-MI (Table 2). Male patients were more likely to receive a beta-blocker after MI with an unadjusted OR of 1.67 ($P = 0.021$). Among new users, 78.9% and 4.8% of patients were white and black, respectively, compared to 73.6% and 10.9% in the non-

users group ($P = 0.115$). In the unadjusted bivariable analyses, patients with congestive heart failure (OR: 0.33; $P < 0.001$), cardiac arrhythmia (OR: 0.39; $P = 0.001$), chronic pulmonary disease (OR: 0.58; $P = 0.041$), renal failure (OR: 0.35; $P = 0.004$), and fluid and electrolyte disorder (OR: 0.32; $P = 0.001$) were less likely to receive a beta-blocker within 30 days of MI hospital discharge. When comparing new users to non-users, there was no difference among patients with hypothyroidism (11.4% and 17.2%, respectively; $P = 0.123$). There was a significant difference when comparing number of medication classes being utilized prior to MI between new users and non-users of beta-blockers ($P < 0.001$). Among new users, 53.3% of patients were taking a diabetes medication prior to index MI compared to 43.7% among non-users ($P = 0.076$). Patients taking an ACE inhibitor or ARB (OR: 1.68; $P = 0.026$), a calcium channel blocker (OR: 2.36; $P = 0.028$), or a diuretic (OR: 2.02; $P = 0.008$) were more likely to receive a beta-blocker after hospital discharge as well.

Among the 167 new users in the cohort, the distribution of first beta-blockers utilized follows: 75 patients (44.9%) received metoprolol tartrate, 33 (19.8%) received metoprolol succinate, 51 (30.5%) received carvedilol, and 8 patients (4.8%) received either atenolol, nebivolol, or propranolol. All of these beta-blockers were cardioselective except carvedilol (which also has an ancillary alpha-1 antagonism mechanism of action) and propranolol. None of these beta-blockers had intrinsic sympathomimetic activity (ISA).

Multivariable logistic regression model

All variables from Table 2 were considered for inclusion in the initial multivariable logistic regression model. The comorbidities of pulmonary circulation disorder, liver disease, and obesity were excluded from the initial model because so few patients had these conditions. Additionally, obesity is often not well captured by ICD-9 codes. The antihypertensive classes of vasodilator and other antiadrenergics were combined into one category for inclusion in the model. Due to issues of multicollinearity, it was decided to include only one measure of socioeconomic status in the initial regression model, either college degree or annual income. Whether education or income was included in the initial model, the same final model resulted. The initial model that included income was utilized to fit the model.

The initial multivariable regression model had an AIC of 445.559. After model reduction, the AIC decreased to 421.235 and included the following variables: age, sex, race, congestive heart failure, cardiac arrhythmia, renal failure, depression, fluid and electrolyte disorder, number of medications, calcium channel blocker, and diuretic. Other race compared to white (OR_{adj}: 0.74; CI: 0.38–1.45) was not associated with receipt of a beta-blocker after a MI. However, black patients (OR_{adj}: 0.37; CI: 0.14–0.99) were less likely to receive a beta-blocker compared to white patients; therefore, the race variable was changed to indicate whether the patient was black for further model reductions.

Interactions to investigate in the regression model were based on clinical knowledge and included (1) age with number of medications, (2) race with calcium channel blocker use, (3) congestive heart failure with fluid and electrolyte disorder, (4) congestive heart failure with diuretic use, (5) cardiac arrhythmia with calcium channel

blocker use, (6) renal failure with diuretic use, and (7) depression with number of medications. With the addition of these interaction terms, the AIC was 426.758. The final reduced model had an AIC of 416.904.

The final reduced multivariable regression model including interaction terms can be seen in Table 3. Patients taking 1 to 5 medications prior to index MI (OR_{adj}: 3.59; CI: 1.74–7.38) were significantly more likely to receive a beta-blocker within 30 days post-hospital discharge when compared to patients taking no medications; patients taking calcium channel blockers before index MI were also more likely to receive a beta-blocker after hospital discharge (OR_{adj}: 2.63; CI: 1.05–6.60). Patients with congestive heart failure (OR_{adj}: 0.45; CI: 0.21–0.96) or a cardiac arrhythmia (OR_{adj}: 0.44; CI: 0.23–0.86) were less likely to initiate beta-blocker therapy post-MI. Among patients who were not taking a diuretic prior to index MI, patients with renal failure were less likely to initiate beta-blocker therapy as well (OR_{adj}: 0.17; CI: 0.05–0.65); this association was not seen among patients with renal failure who were taking a diuretic (OR_{adj}: 1.42; CI: 0.35–5.86). The c-statistic for the final fitted regression model was 0.767 (CI: 0.717–0.816). Using the leave-one-out cross-validation method, the c-statistic was reported as 0.719 (CI: 0.665–0.773).

Four sensitivity analyses were run to determine if imputation of missing values significantly impacted the final model. As education and income were the first variables eliminated in their respective models, the first two sensitivity analyses were conducted by excluding patients with missing values for education and income, respectively. In these two models, all point estimates had less than 10% relative change except fluid and electrolyte disorder and polypharmacy decreased 12.5% and 10.3%, respectively, in the

education model and congestive heart failure increased 11.1% in the income model. Two other sensitivity analyses were conducted by excluding the one patient with a missing value for race and changing the value of race to black. In the first sensitivity analysis, all point estimates had less than 10% relative change except renal failure among patients taking diuretics decreased 12.7%. When the race for that single patient was changed to black, no significant relative changes in point estimates occurred except a 13.6% increase in the black variable. The c-statistic changed less than 1% in all four sensitivity analyses.

Conclusions

Despite recommendations from clinical guidelines, beta-blocker treatment continues to be underutilized in type 2 diabetic patients in the setting of secondary MI prevention. Only 49.0% of 341 patients in this study had a beta-blocker prescription claim within 30 days after their hospital discharge; this is similar to rates of beta-blocker treatment in this population previously reported.[3] Even in this relatively young post-MI population, age was an important factor in bivariable analyses and was included in the final model. Age was trending towards significance in the final regression model, signifying that power may not have been met. Similarly, the best-fit model had sex in it although it was not significant; male patients may have been found to be more likely to initiate beta-blocker therapy in this setting if the cohort had been larger. Race also appeared to be a significant predictor of initiating beta-blocker therapy in this population until interaction terms were added to the model; it is possible that power was not met due to the low number of non-white patients in our cohort. Black patients with type 2 diabetes

may be significantly less likely to initiate beta-blocker therapy after MI, and this association should be further evaluated in a more diverse population.

The strongest predictor of initiating beta-blocker therapy was number of medications filled within the 90 days prior to index MI; however, patients filling 6 or more medications in this period were no more likely to initiate a beta-blocker than patients taking no medications. It is not surprising that patients with a chronic condition such as diabetes who were taking no medications previously would be less likely to initiate a new preventative therapy. However, it is not clear why patients with no medications had similar rates of initiation compared to patients with 6 or more medications. Polypharmacy may be related to pill burden and patients not wanting to initiate a new therapy; it could also be related to drug interactions and safety concerns associated with the initiation of a beta-blocker. Patients taking a calcium channel blocker prior to MI were also more likely to initiate beta-blocker therapy. This may be related to patient behavior because the percent of patients taking other preventative therapies was higher in the new users group for all medications except vasodilators in the bivariable analyses.

Patients with a history of cardiac arrhythmia were less likely to initiate therapy. This could be related to the antiarrhythmic effects of beta-blockers and the potential to worsen this comorbidity with the addition of a beta-blocker if the patient was already controlled on another antiarrhythmic medication. The use of diuretics may have served as a proxy for the severity of renal failure in the interaction within our model as diuretics are typically not recommended in patients with severe renal failure. While renal insufficiency is an important consideration for many drug therapies, this finding is interesting given

that most beta-blockers, including metoprolol and carvedilol, are not significantly eliminated in the urine before hepatic metabolism. Among patients not taking diuretics prior to index MI, renal failure patients were significantly less likely to initiate beta-blocker therapy. This association was not present when considering patients who were taking a diuretic prior to index MI. It is interesting to note that although not always statistically significant, new users had smaller percentages of patients among all comorbidities except pulmonary circulation disorder and liver disease in the bivariable analyses. This again seems to align with the healthy user phenomenon.

This study confirms previous findings that beta-blockers are underutilized among patients with type 2 diabetes for secondary prevention of MI[3,14,15] despite current recommendations.[1,2,11] Male patients have also been shown to be more likely than females to receive beta-blockers among this population.[3] To our knowledge, this is the only observational study that has evaluated initiation of beta-blocker therapy in this population while adjusting for other medication therapy, including number and classes of medication. This is also the only study to investigate beta-blocker initiation in a type 2 diabetes post-MI population with a mean age less than 65.

Some limitations exist in our study. First, lab values were not available for a majority of patients near the time of hospital discharge. This is a common limitation in studies utilizing administrative claims data. Clinical decisions in diabetic patients rely heavily on glycemic control and this information may have provided added predictive value for our model. Secondly, our study could not account for prescriptions filled outside of coverage. The trend of marketing out-of-pocket low-cost prescription medications began in 2006 and included both metoprolol and carvedilol by the end of

2007.[19] This creates a potential for misclassification bias. However, among the 167 new users of beta-blockers in our study, 7.8, 22.8, and 69.5% of patients had a co-pay of $0, between $0 and $4, and more than $4, respectively, when standardized to a 30-day supply. When these co-pay categories were stratified by income, 60.9, 65.5, and 79.2% of patients were paying more than $4 for a 30-day supply of a beta-blocker in the low-, middle-, and high-income categories, respectively. With such a high proportion of patients paying more than $4 per 30-day supply for a beta-blocker, $4 prescriptions may not have affected the behavior of patients with prescription insurance. In addition, excluding patients with no prescription claims in the entire study period may keep some of these patients out of the study population. Finally, we were not able to detect if patients were non-users because they were not prescribed a beta-blocker or because they chose not to fill a prescription they received after hospital discharge. Identifying whether patients received beta-blocker treatment is more important than why they did or did not receive the medication when evaluating outcomes related to this treatment; however, if post-MI beta-blocker therapy in patients with type 2 diabetes is indeed beneficial, identifying why patients are not receiving this therapy is an important step in solving the issue of underutilization.

However, our study also possesses several strengths. Unlike previous research, our study adjusted for the number and types of medications when evaluating initiation of beta-blockers among this population. This is an important factor in better understanding the behavior of both prescribers and patients. Also, cross-validation was conducted to show the anticipated predictive power of our model if used with a different dataset in a

similar population. Finally, the inclusion of patients with only continuous eligibility and at least 6 months of data prior to index MI reduced the likelihood of bias.

The predictors identified in our final model set a strong foundation for future investigations of the outcomes associated with the use of beta-blockers in this population. If (1) the variables are available and reliable, and (2) the variables are related to the outcome of interest, all variables in our final model should be considered for adjustment in observational studies examining outcomes related to beta-blocker therapy in this population. Our study also confirms the results from previous researchers that beta-blockers are underutilized in this population. The results from this study could help clinicians and policymakers determine if more patients with type 2 diabetes should be receiving beta-blocker therapy post-MI and could assist in developing interventions targeted to patients less likely to receive this therapy.

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RH certifies that he will take public responsibility for the content and provide any relevant data upon request. This research in full has not been published elsewhere and does not overlap or duplicate any previous work. Initial iterations of this research were presented in poster format at the ASHP Midyear Clinical Meeting in 2013, the ISPOR Annual International Meeting in 2014, and the Rho Chi Research Day at the University of Kentucky College of Pharmacy in 2014.

Figure 1 – *Selection of study cohort*

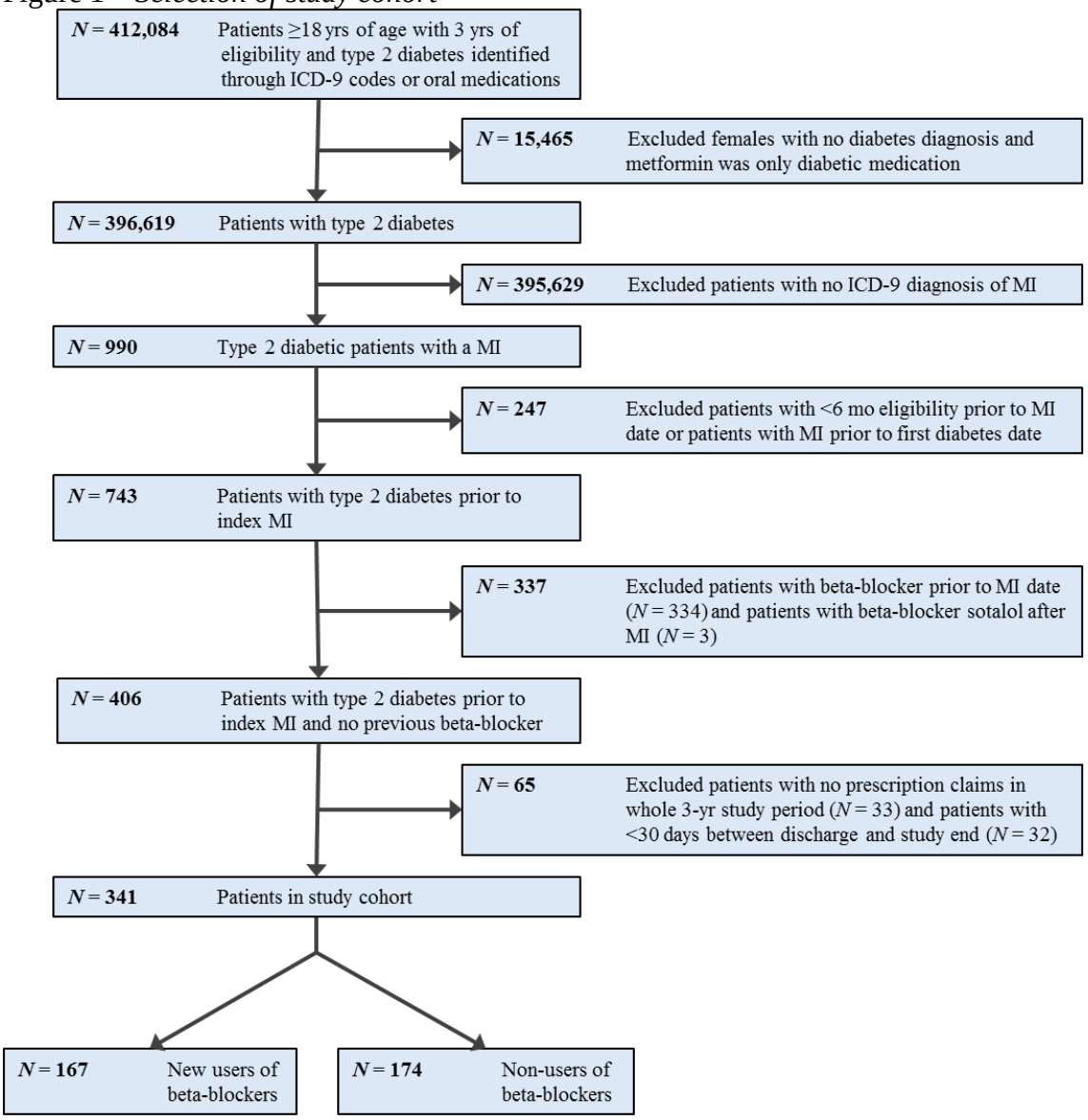

Table 1 – *Cohort characteristics*

Patient characteristics	*N* = 341
Age (years)	63.3 ± 13.1
Sex	
Male	199 (58.4)
Female	142 (41.6)
Race*	
White	259 (76.2)
Black	27 (7.9)
Other	54 (15.9)
College degree†	64 (19.2)
Annual household income‡	
Less than $30,000	56 (17.5)
$30,000 to $74,999	173 (54.1)
$75,000 or More	91 (28.4)
U.S. Census geographic region	
Midwest	77 (22.6)
Northeast	31 (9.1)
South	191 (56.0)
West	42 (12.3)
Comorbidities	
Congestive heart failure	55 (16.1)
Cardiac arrhythmia	74 (21.7)
Valvular disease	37 (10.9)
Pulmonary circulation disorder	9 (2.6)
Peripheral vascular disorder	51 (15.0)
Hypertension	228 (66.9)
Chronic pulmonary disease	73 (21.4)
Hypothyroidism	49 (14.4)
Renal failure	40 (11.7)
Liver disease	10 (2.9)
Obesity	15 (4.4)
Depression	33 (9.7)
Fluid and electrolyte disorder	49 (14.4)
Blood glucose testing strips	67 (19.7)
Number of medications	
None	62 (18.2)
1 to 5	123 (36.1)
6 or more	156 (45.8)
Any diabetes medication	165 (48.4)
Sulfonylurea or meglitinide	63 (18.5)
Insulin	69 (20.2)
Antihypertensive medications	
ACE inhibitor or ARB	111 (32.6)
Calcium channel blocker	31 (9.1)
Diuretic	77 (22.6)
Vasodilator	12 (3.5)
Other antiadrenergic	39 (11.4)
Statin	130 (38.1)
Beta-blocker post-MI	167 (49.0)

Data are means ± SD or *N* (%). All characteristics are pre-MI except beta-blocker exposure. * Adds up to 340 due to 1 missing value. † Adds up to 333 due to 8 missing values. ‡ Adds up to 320 due to 21 missing values.

Table 2 – *Characteristics of new users and non-users of beta-blockers*

Patient characteristics	New users of beta-blockers (*N* = 167)	Non-users of beta-blockers (*N* = 174)	*P* value
Age (years)	61.1 ± 11.1	65.3 ± 14.5	0.003 §
Sex			0.021
Male	108 (64.7)	91 (52.3)	
Female	59 (35.3)	83 (47.7)	
Race *			0.115
White	131 (78.9)	128 (73.6)	
Black	8 (4.8)	19 (10.9)	
Other	27 (16.3)	27 (15.5)	
College degree †	33 (20.5)	31 (18.0)	0.567
Annual household income ‡			0.388
Less than $30,000	23 (14.8)	33 (20.0)	
$30,000 to $74,999	84 (54.2)	89 (53.9)	
$75,000 or More	48 (31.0)	43 (26.1)	
U.S. Census geographic region			0.075
Midwest	37 (22.2)	40 (23.0)	
Northeast	22 (13.2)	9 (5.2)	
South	90 (53.9)	101 (58.1)	
West	18 (10.8)	24 (13.8)	
Comorbidities			
Congestive heart failure	15 (9.0)	40 (23.0)	<0.001
Cardiac arrhythmia	23 (13.8)	51 (29.3)	0.001
Valvular disease	13 (7.8)	24 (13.8)	0.075
Pulmonary circulation disorder	6 (3.6)	3 (1.7)	0.328 ‖
Peripheral vascular disorder	22 (13.2)	29 (16.7)	0.366
Hypertension	106 (63.5)	122 (70.1)	0.193
Chronic pulmonary disease	28 (16.8)	45 (25.9)	0.041
Hypothyroidism	19 (11.4)	30 (17.2)	0.123
Renal failure	11 (6.6)	29 (16.7)	0.004
Liver disease	6 (3.6)	4 (2.3)	0.535 ‖
Obesity	7 (4.2)	8 (4.6)	0.855
Depression	11 (6.6)	22 (12.6)	0.059
Fluid and electrolyte disorder	13 (7.8)	36 (20.7)	0.001
Blood glucose testing strips	36 (21.6)	31 (17.8)	0.385
Number of medications			<0.001
None	19 (11.4)	43 (24.7)	
1 to 5	76 (45.5)	47 (27.0)	
6 or more	72 (43.1)	84 (48.3)	
Any diabetes medication	89 (53.3)	76 (43.7)	0.076
Sulfonylurea or meglitinide	37 (22.2)	26 (14.9)	0.086
Insulin	35 (21.0)	34 (19.5)	0.745
Antihypertensive medications			
ACE inhibitor or ARB	64 (38.3)	47 (27.0)	0.026
Calcium channel blocker	21 (12.6)	10 (5.8)	0.028
Diuretic	48 (28.7)	29 (16.7)	0.008
Vasodilator	5 (3.0)	7 (4.0)	0.606
Other antiadrenergic	20 (12.0)	19 (10.9)	0.759
Statin	69 (41.3)	61 (35.1)	0.234

Data are means ± SD or *N* (%). All characteristics are pre-MI except beta-blocker exposure. All *P* values based on chi-square statistic except where denoted. * Adds up to 340 due to 1 missing value. † Adds up to 333 due to 8 missing values. ‡ Adds up to 320 due to 21 missing values. § Two-sample t-test statistic. ‖ Fisher's exact test statistic.

Table 3 – *Multivariable logistic regression model predicting initiation of beta-blocker after myocardial infarction among patients with type 2 diabetes*

Patient characteristics	Adjusted OR (95% CI)
Age	0.98 (0.96–1.00)
Male	1.50 (0.91–2.47)
Black*	0.44 (0.16–1.19)
Congestive heart failure	0.45 (0.21–0.96)
Cardiac arrhythmia	0.44 (0.23–0.86)
Depression	0.50 (0.22–1.17)
Fluid and electrolyte disorder	0.48 (0.21–1.13)
Renal failure	
No diuretic	0.17 (0.05–0.65)
Taking a diuretic	1.42 (0.35–5.86)
Number of medications	
None	Referent
1 to 5	3.59 (1.74–7.38)
6 or more	1.46 (0.70–3.05)
Calcium channel blocker	2.63 (1.05–6.60)

All characteristics are pre-MI except beta-blocker exposure. All variables from Table 2 were included in initial model except college degree, pulmonary circulation disorder, liver disease, and obesity. In the initial model, vasodilator and other antiadrenergic were combined into other antihypertensive category. For race, 1 patient with a missing value was placed in the "Other" category. For annual household income, 21 patients with missing values were placed in $30,000 to $74,999 category.
*Based on the results before inclusion of interactions terms, the variable for race was changed to a variable indicating whether the patient was black.

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