Predictors of β -Blocker Initiation After Myocardial Infarction in Patients With Type 2 Diabetes: A Retrospective Study of a Privately Insured US Population

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Abstract

Background: Beta-blockers remain important for secondary prevention after myocardial infarction (MI). Despite clinical guideline recommendations, underutilization of this pharmacotherapy continues in patients with type 2 diabetes (T2DM) compared to the general post-MI population. **Objective:** This study aimed to (1) quantify the proportion of T2DM patients utilizing β -blocker therapy within 30 days of hospital discharge after MI and (2) identify clinical and demographic characteristics predicting initiation of β -blocker therapy. **Methods:** A retrospective cohort of US employed, commercially insured individuals was assembled using de-identified enrollment files, medical claims, and pharmacy claims from 2007 to 2009. Inclusion criteria were the following: (1) type 2 diabetes, (2) ≥ 18 years old, (3) continuous eligibility, (4) MI. Multivariable logistic regression with adjusted odds ratios (OR_{adj}) using manual backward elimination was used to identify predictors of β -blocker initiation within 30 days of discharge from index hospitalization. **Results:** Of 341 T2DM patients, 167 (49.0%) were new users and 174 (51.0%) were nonusers of β -blockers within 30 days of post-MI hospital 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 β -blockers post-MI. Patients with heart failure (OR_{adj} 0.45) or an arrhythmia (OR_{adj} 0.44) were less likely to initiate β -blockers as well as patients with renal failure not taking a diuretic (OR_{adj} 0.17). **Conclusions:** These results confirm previous findings that β -blockers are underutilized in T2DM patients post-MI. Predictors from the regression model can guide future research investigating how this deviation from guidelines is attributed to prescriber versus patient behavior.

Keywords

myocardial infarction, type 2 diabetes, β -adrenergic blockers, standards of practice, preventative medicine

Introduction

Beta-blockers are effective in decreasing myocardial ischemia, re-infarction, and the frequency of complex ventricular dysrhythmias as well as increasing long-term survival, which supports their key role in secondary prevention after myocardial infarction (MI).^{1,2} Current guidelines from the American Heart Association recommend initiation of oral β -blockers within 24 hours of an MI.^{1,3} However, β -blockers have a history of relative contraindication in diabetic patients based on their potential to mask the warning signs of hypoglycemia⁴⁻⁶ and negatively impact glycemic control.⁶⁻⁹ This brings about somewhat of a paradox. On one hand, patients with type 2 diabetes (T2DM) have worse cardiovascular outcomes after MI,^{6,10} suggesting they may have more to gain from cardioprotective therapies like β -blockers. On the other hand, cardiovascular outcomes in diabetic patients are often improved through tight glycemic control,⁷ which may be worsened by β -blockers.

Although current American Diabetes Association guidelines recommend β -blockers in T2DM patients after MI,¹¹ most information regarding β -blocker utilization in this population^{4,8,12-17} comes from subgroup and post hoc analyses. An observational study using 1990s Canadian data found that 43% of T2DM patients without previous exposure received β -blockers after an MI.⁴ In the Netherlands, 60% of post-MI T2DM patients were prevalent users of β -blockers.¹⁷ A recent MI-registry study across 24 US hospitals found that 93% of diabetic patients were prescribed β -blockers at hospital discharge.⁸ This study captures important information on prescribers' behavior but no data

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on whether prescriptions were filled by the patients. A longitudinal study found T2DM patients had better adherence to β -blockers but increased risk of subsequent cardiovascular events after acute coronary syndrome compared to patients without diabetes.¹⁸ Patients taking medications that increase the risk of hypoglycemia may be even less likely to receive β -blockers after MI.^{14,15}

Few studies have evaluated β -blocker utilization post-MI specifically among T2DM patients in the United States.^{14,15,19} The purpose of this study was to (1) quantify the proportion of T2DM patients utilizing β -blocker therapy within 30 days of hospital discharge post-MI and (2) identify clinical and demographic factors of T2DM patients predicting initiation of β -blocker therapy post-MI.

Methods

Data Source

Data included de-identified information on a nationally representative sample of 15 million employed, commercially insured individuals with dependents. The de-identified data set included insurance enrollment files as well as medical (inpatient and outpatient), lab, and pharmacy claims between January 2007 and December 2009. Data use was approved by the University of Kentucky Institutional Review Board, which oversees the ethical conduct of research at this institution. Given that all data were previously collected for purposes other than research and were de-identified, informed consent was not required.

Study Design

We identified a retrospective cohort of patients with T2DM that were hospitalized and discharged with an MI diagnosis during our study period. For patients with multiple qualifying hospitalizations, only the first was considered for analysis. The hospital admission date for the first eligible MI diagnosis code was used as the index date. The 6-month period prior to the index date was used to identify comorbidities and to exclude patients with previous β -blocker exposure. Medications used by the patient pre-MI were determined using pharmacy claims during the 90 days prior to the index date. Beta-blocker initiation after MI was evaluated from the index date to 30 days post-MI discharge.

Study Population

The following inclusion criteria were used to identify patients for our study: (1) International Classification of Diseases, 9th Clinical Modification (ICD-9-CM) diagnosis codes for T2DM in medical claims (any diagnosis position on the claim) or pharmacy prescription claims for oral

diabetes medications identified through National Drug Codes (NDCs), (2) at least 18 years of age, (3) continuous eligibility through the entire study period, and (4) ICD-9-CM codes for MI at hospital discharge (410.X1 as primary or secondary diagnosis).

Exclusion criteria included (1) females lacking T2DM diagnosis code and receiving metformin as the exclusive oral diabetes medication, (2) less than 6 months of eligibility prior to index MI, (3) MI identified prior to T2DM, (4) β -blocker prescription claim in the 6 months prior to index MI, (5) first post-MI β -blocker was sotalol, (6) no prescription claims for entire study period, and (7) less than 30 days between index discharge date and study conclusion. Female patients without T2DM diagnosis and receiving only metformin were excluded to prevent misclassification of patients with polycystic ovary syndrome. Sotalol was excluded as it is not indicated for secondary prevention of MI (see Figure 1 for cohort selection).

Variables of Interest

Potential predictors of β -blocker receipt included demographic and clinical characteristics as well as measures of health care utilization at baseline (pre-MI). Demographic characteristics investigated were age, sex, race, and proxy measures of socioeconomic status including education, annual household income, and geographic region. Clinical characteristics included baseline comorbidities and medications. Comorbidities were identified through the Elixhauser Comorbidity algorithm for the 6 months preceding MI²⁰ (see Table 1 for a full list of comorbidities). Patients currently taking insulin or insulin secretagogues (sulfonylureas and meglitinides) were identified, as these patients are likely at a higher risk of hypoglycemia. Additionally, patients taking any diabetes medication, including insulin, were identified, as well as patients taking other medications that could lower blood pressure. Statin users were identified to evaluate whether patients already taking post-MI recommended therapy were more likely to initiate β -blockers.

The number of prescription medications filled 90 days before index hospitalization was a proxy 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 or non-pharmacologic products were not included in this count. Unique AHFS codes were counted as the number of prescription medications received pre-MI. Patients with a prescription claim for blood glucose testing strips 90 days prior to MI were identified, as some clinicians have stated that

Figure 1. Selection of study cohort from 2007 to 2009 patient enrollment files and claims data.

ICD-9, International Classification of Diseases, 9th Clinical Modification; MI, myocardial infarction; mo, month(s); yr, year(s)

diabetic patients who self-monitor blood glucose may be better candidates for post-MI β -blocker therapy.⁶

Study Endpoint

The endpoint of interest was a prescription claim for a β -blocker within 30 days after hospital discharge. Beta-blockers (including combination products) were identified using AHFS code 242400. Patients who initiated β -blockers between index date and 30 days post-hospital discharge were considered new users of β -blockers. All other patients were classified as nonusers.

Statistical Analysis

Population characteristics were summarized using mean and standard deviation (SD) for continuous variables and percent of the total for categorical variables. Bivariable

statistics were used to compare new users to nonusers of β -blockers with regard to baseline characteristics and included either a 2-sample *t* test, χ^2 test, or Fisher's exact test as appropriate.

A multivariable logistic regression model was utilized to predict initiation of β -blockers among T2DM patients after MI. All variables from bivariable analyses were considered in the initial model. When few patients had positive values for indicator variables, the variable was either eliminated from the regression or combined with a similar variable to improve statistical efficiency. Missing values for race were added to the "Other" category ($N < 5$), and missing values for other variables were replaced with the mode to allow patient inclusion in the regression analysis ($N = 8$ [2.3%] and $N = 21$ [6.2%] for education and income, respectively). To avoid issues of multicollinearity, only one measure of socioeconomic status was included in the initial regression model; therefore, 2 separate models were tested, one with income

Table 1. Cohort Characteristics of Patients With Type 2 Diabetes After Myocardial Infarction (MI)^a.

Patient Characteristics (N = 341)	
Age (years)	63.3 [13.1]
Sex	
Male	199 (58.4)
Female	142 (41.6)
Race ^b	
White	259 (76.2)
Black	27 (7.9)
Other	54 (15.9)
College degree ^c	64 (19.2)
Annual household income ^d	
Less than \$30 000	56 (17.5)
\$30 000 to \$74 999	173 (54.1)
\$75 000 or more	91 (28.4)
US 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/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)
β-Blocker post-MI	167 (49.0)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MI, myocardial infarction.

^aData are mean [SD] or n (%). All characteristics are pre-myocardial infarction except β-blocker exposure.

^bAdds up to 340 due to 1 missing value.

^cAdds up to 333 due to 8 missing values.

^dAdds up to 320 due to 21 missing values.

and another with education. Manual backward elimination was used to identify the best model using the Akaike information criterion (AIC) for model selection. After model reduction, variables remaining in the model were evaluated for interactions by adding interaction terms and using a similar manual backward elimination technique.

Adjusted odds ratios (OR_{adj}) with 95% confidence intervals (CIs) were reported for all variables in the regression models. Internal validation of the final predictive model was completed using leave-one-out cross-validation.²¹ All statistical analyses were completed using SAS software (Version 9.4 for Windows, SAS Institute, Cary, NC).

Results

Out of 396 619 patients with T2DM, 743 patients had an MI during the 2007 to 2009 study period (Figure 1). After applying eligibility criteria, 341 patients were included in the study cohort. Of these, 167 (49.0%) and 174 (51.0%) patients were identified as post-MI new users and nonusers of β-blockers, respectively. Among new users, the most common β-blockers were metoprolol tartrate (N = 75; 44.9%), metoprolol succinate (N = 33; 19.8%), and carvedilol (N = 51; 30.5%).

The mean age in the cohort was 63.3 years (Table 1). A majority of patients were white (76.2%) and male (58.4%). The most common comorbidities identified pre-MI were hypertension (66.9%), cardiac arrhythmia (21.7%), and chronic pulmonary disease (21.4%). The most common antihypertensives were (1) angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs; N = 111; 32.6%) and (2) diuretics (N = 77; 22.6%).

New users (mean [SD]: 61.1 [11.1]) were younger than nonusers (65.3 [14.5]; *P* = .003) and more likely to be male (*P* = .021; Table 2). Black patients were less likely to be new users (*P* = .115). In unadjusted analyses, patients with congestive heart failure (OR = 0.33; *P* < .001), cardiac arrhythmia (OR = 0.39; *P* = .001), chronic pulmonary disease (OR = 0.58; *P* = .041), renal failure (OR = 0.35; *P* = .004), and fluid/electrolyte disorder (OR = 0.32; *P* = .001) were less likely to receive a β-blocker within 30 days of hospital discharge (Tables 2 and 3). Among new users, 53.3% of patients were taking a diabetes medication prior to index MI compared to 43.7% of nonusers (*P* = .076). Patients taking an ACE inhibitor or ARB (OR = 1.68; *P* = .026), a calcium channel blocker (OR = 2.36; *P* = .028), or a diuretic (OR = 2.02; *P* = .008) were more likely to be new users of β-blockers after hospital discharge.

Multivariable Logistic Regression Model

Indicators of pulmonary circulation disorder, liver disease, and obesity were excluded from the regression model given

Table 2. Characteristics of New Users and Nonusers of β -Blockers After Myocardial Infarction Among Patients With Type 2 Diabetes^a.

Patient Characteristics	New Users of β -Blockers (N = 167)	Nonusers of β -Blockers (N = 174)	P
Age (years)	61.1 [11.1]	65.3 [14.5]	.003 ^b
Sex			.021
Male	108 (64.7)	91 (52.3)	
Female	59 (35.3)	83 (47.7)	
Race ^c			.115
White	131 (78.9)	128 (73.6)	
Black	8 (4.8)	19 (10.9)	
Other	27 (16.3)	27 (15.5)	
College degree ^d	33 (20.5)	31 (18.0)	.567
Annual household income ^e			.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)	
US Census geographic region			.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)	<.001
Cardiac arrhythmia	23 (13.8)	51 (29.3)	.001
Valvular disease	13 (7.8)	24 (13.8)	.075
Pulmonary circulation disorder	6 (3.6)	3 (1.7)	.328 ^f
Peripheral vascular disorder	22 (13.2)	29 (16.7)	.366
Hypertension	106 (63.5)	122 (70.1)	.193
Chronic pulmonary disease	28 (16.8)	45 (25.9)	.041
Hypothyroidism	19 (11.4)	30 (17.2)	.123
Renal failure	11 (6.6)	29 (16.7)	.004
Liver disease	6 (3.6)	4 (2.3)	.535 ^f
Obesity	7 (4.2)	8 (4.6)	.855
Depression	11 (6.6)	22 (12.6)	.059
Fluid/electrolyte disorder	13 (7.8)	36 (20.7)	.001
Blood glucose testing strips	36 (21.6)	31 (17.8)	.385
Number of medications			<.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)	.076
Sulfonylurea or meglitinide	37 (22.2)	26 (14.9)	.086
Insulin	35 (21.0)	34 (19.5)	.745
Antihypertensive medications			
ACE inhibitor or ARB	64 (38.3)	47 (27.0)	.026
Calcium channel blocker	21 (12.6)	10 (5.8)	.028
Diuretic	48 (28.7)	29 (16.7)	.008
Vasodilator	5 (3.0)	7 (4.0)	.606
Other antiadrenergic	20 (12.0)	19 (10.9)	.759
Statin	69 (41.3)	61 (35.1)	.234

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MI, myocardial infarction.

^aData are mean [SD] or N (%). All characteristics are pre-myocardial infarction except β -blocker exposure. All P values based on χ^2 statistic except where denoted.^bTwo-sample t test statistic.^cAdds up to 340 due to 1 missing value.^dAdds up to 333 due to 8 missing values.^eAdds up to 320 due to 21 missing values.^fFisher's exact test statistic.

Table 3. Logistic Regression Models Predicting Initiation of β -Blocker After Myocardial Infarction Among Patients with Type 2 Diabetes^a.

Patient Characteristics	Unadjusted, OR (95% CI)	Full Model, AOR (95% CI)	Reduced Model, AOR (95% CI)
Age	0.98 (0.96-0.99)	0.98 (0.96-1.00)	0.98 (0.96-1.00)
Male	1.67 (1.08-2.58)	1.45 (0.85-2.47)	1.50 (0.91-2.47)
Race ^b			
White	Referent	Referent	Referent
Black	0.41 (0.17-0.97)	0.37 (0.13-1.04)	0.44 (0.16-1.19)
Other	1.01 (0.57-1.81)	0.75 (0.38-1.50)	Referent
Annual household income			
Less than \$30 000	0.71 (0.39-1.30)	0.93 (0.44-1.96)	
\$30 000 to \$74 999	Referent	Referent	
\$75 000 or more	1.14 (0.69-1.88)	1.08 (0.55-1.94)	
US Census geographic region			
Midwest	1.04 (0.61-1.76)	1.03 (0.55-1.94)	
Northeast	2.74 (1.20-6.26)	1.94 (0.75-5.03)	
South	Referent	Referent	
West	0.84 (0.43-1.65)	0.88 (0.40-1.94)	
Congestive heart failure	0.33 (0.18-0.63)	0.43 (0.20-0.95)	0.45 (0.21-0.96)
Cardiac arrhythmia	0.39 (0.22-0.67)	0.46 (0.22-0.94)	0.44 (0.23-0.86)
Valvular disease	0.53 (0.26-1.08)	1.19 (0.45-3.10)	
Peripheral vascular disorder	0.76 (0.42-1.38)	1.25 (0.60-2.61)	
Hypertension	0.74 (0.47-1.16)	0.82 (0.46-1.45)	
Chronic pulmonary disease	0.58 (0.34-0.98)	0.68 (0.35-1.32)	
Hypothyroidism	0.62 (0.33-1.14)	1.05 (0.49-2.22)	
Renal failure	0.35 (0.17-0.73)	0.38 (0.15-0.96)	
No diuretic			0.17 (0.05-0.65)
Taking a diuretic			1.42 (0.35-5.86)
Depression	0.49 (0.23-1.04)	0.49 (0.20-1.18)	0.50 (0.22-1.17)
Fluid/electrolyte disorder	0.32 (0.17-0.64)	0.56 (0.24-1.34)	0.48 (0.21-1.13)
Blood glucose test strips	1.27 (0.74-2.17)	1.24 (0.62-2.50)	
Number of medications			
None	Referent	Referent	Referent
1 to 5	3.66 (1.91-7.01)	3.40 (1.52-7.57)	3.59 (1.74-7.38)
6 or more	1.94 (1.04-3.62)	1.46 (0.55-2.66)	1.46 (0.70-3.05)
Any diabetes medication	1.47 (0.96-2.26)	0.88 (0.40-1.96)	
Sulfonylurea or meglitinide	1.62 (0.93-2.82)	1.20 (0.54-2.66)	
Insulin	1.09 (0.64-1.85)	0.77 (0.35-1.71)	
Antihypertensive medications			
ACE inhibitor or ARB	1.68 (1.06-2.65)	1.41 (0.73-2.73)	
Calcium channel blocker	2.36 (1.08-5.17)	2.43 (0.92-6.38)	2.63 (1.05-6.60)
Diuretic	2.02 (1.20-3.40)	3.04 (1.52-6.07)	
Other antihypertensives	1.05 (0.57-1.93)	1.57 (0.71-3.51)	
Statin	1.30 (0.84-2.02)	0.88 (0.40-1.96)	

Abbreviations: OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MI, myocardial infarction.

^aAll characteristics are pre-myocardial infarction except β -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 other category. For annual household income, 21 patients with missing values were placed in \$30 000 to \$74 999 category.

^bBased on the results before inclusion of interaction terms, the variable for race was changed to a variable indicating whether the patient was black.

the small number of patients with these conditions; the antihypertensive classes of vasodilator and other antiadrenergics were also combined into one category to increase

statistical efficiency. Whether education or income was included in the initial model, the same final model resulted. For all variables included in regression analyses, the OR

and OR_{adj} can be seen in the unadjusted and full models, respectively (Table 3).

After initial model reduction, the “Other” race category compared to white ($OR_{adj} = 0.74$; $CI = 0.38-1.45$) was not associated with receipt of a β -blocker after an MI. However, black patients ($OR_{adj} = 0.37$; $CI = 0.14-0.99$) were less likely to receive a β -blocker compared to white patients; therefore, the race variable was changed to indicate whether the patient was black.

Interaction terms evaluated in the regression model included (1) age with number of medications, (2) race with calcium channel blocker use, (3) congestive heart failure with fluid/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. After manual backward elimination, the final reduced model included the interaction term between renal failure and diuretic use (Table 3).

Patients taking 1 to 5 medications prior to index MI ($OR_{adj} = 3.59$; $CI = 1.74-7.38$) and patients taking calcium channel blockers ($OR_{adj} = 2.63$; $CI = 1.05-6.60$) prior to index MI were more likely to be new users. 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 be new users. Among patients who were not taking a diuretic prior to index MI, patients with renal failure were less likely to initiate β -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 area under the curve (AUC) for the final regression model was 0.767 ($CI = 0.717-0.816$). Using leave-one-out cross-validation, the resulting AUC was 0.719 ($CI = 0.665-0.773$).

Discussion

Despite recommendations from clinical guidelines, only 49.0% of 341 T2DM patients had a β -blocker prescription claim within 30 days after hospital discharge. A 1990s US study estimated that 28% to 33% of patients with diabetes received a prescription for β -blockers at post-MI hospital discharge compared to 36% of patients without diabetes.¹⁵ Another US study of low-income, elderly, general post-MI patients estimated that β -blocker initiation increased from 42% in 1995 to 72% in 2004.²² Data from a 2007 to 2009 privately insured cohort was used to evaluate post-MI outcomes and found that only 55% of patients with diabetes were adherent to β -blockers for the 180 days post-MI.²³

Our study identified potential predictors of β -blocker initiation after MI specific to patients with T2DM. Interestingly, patients taking 1 to 5 medications pre-MI were likely to initiate β -blocker therapy post-MI while patients taking 6 or more medications were no more likely

to initiate a β -blocker than patients taking no medications. It is not surprising that patients with a chronic condition such as diabetes who were previously taking no medications 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.

Patients with a history of cardiac arrhythmia were less likely to initiate β -blocker therapy. The antiarrhythmic effects of β -blockers could adversely affect patients with a well-controlled arrhythmia. Among patients not taking diuretics, patients with renal failure were less likely to initiate β -blockers. Many diuretics are not recommended in severe renal failure; this interaction, therefore, may have been a proxy for this condition. However, loop diuretics are often clinically indicated in end-stage renal disease,²⁴ possibly implying that this interaction signifies something else. To investigate this further, one would need to evaluate interactions between renal failure and specific classes of diuretics, which would require a larger patient sample than available in our study. This is interesting since most β -blockers are not renally eliminated, and it is unclear whether prescriber or patient behavior is the reason for this finding.

Although not always statistically significant, new users were typically less likely to have comorbidities and more likely to be taking other medications in unadjusted analyses. Patients with chronic conditions already taking medications (especially preventative therapies) may be the ones that exhibit more health-seeking behaviors as compared to patients with similar comorbidities but not taking medications. Previous research has found that, by participating in other health-enhancing activities,²⁵ these “healthy users” are the ones more likely to initiate a new preventative therapy and, thus, may be more likely to initiate β -blocker therapy after MI. Another explanation is that clinicians may be less likely to prescribe β -blockers in patients with multiple comorbidities for fear of increased risk for adverse drug events.

Although age, sex, race, depression, and fluid/electrolyte disorder were not statistically significant in the final model, their inclusion improved the overall fit of the regression model. A lack of power from the small number of eligible patients could be a reason these predictors of β -blocker initiation did not reach statistical significance. Race was a significant predictor of β -blocker initiation in bivariable analyses, but our population being predominantly white decreased the power to detect differences in race in the reduced model. Male diabetic patients have been shown in previous research to be more likely than females to receive β -blockers among the post-MI population.⁴ Also, older age and depression have been shown to predict underuse of medications in the year after discharge for acute coronary syndromes.²⁶ Therefore, these variables should continue to

be investigated among post-MI patients with T2DM in a larger, more diverse population.

Strengths and Limitations

Our study possesses several strengths. Unlike previous research, our study adjusted for number and types of medications when evaluating β -blocker initiation among post-MI T2DM patients. Also, cross-validation was conducted to show the anticipated predictive power of our model if used with a different data set in a similar population. While our findings are not generalizable to the older US Medicare population, they are important to consider as this younger, potentially healthier population may have even more to benefit from secondary prevention after MI.

Some limitations existed in our study. First, because administrative claims data were used for billing purposes and not designed for research, the possibility of variable misclassification existed. Our approach followed the existing standards in the field of using secondary claims data for observational health services and outcomes research. Also, the claims data used in this study were from a commercially insured population, and results may not be generalizable to publicly insured populations.

Second, our study could not account for prescriptions filled outside of coverage. Generic drug discount programs (GDDPs) were introduced to the US market in 2006²⁷ and included metoprolol and carvedilol by 2007.²⁸ A survey among predominantly insured patients found that only 4.7% of respondents used a GDDP in 2008,²⁹ and the use of these programs was likely greater in uninsured populations.^{27,29} Our exclusion of patients with no prescription claims during the entire study may partially address this potential misclassification bias.

Finally, we were not able to detect if patients were non-users because they were not prescribed a β -blocker or because they chose not to fill a prescription, an important distinction in addressing underutilization of this therapy. Data evaluating β -blocker utilization post-MI using hospital medical records found that β -blocker initiation rates were much higher (82%), even among diabetic patients.¹⁴ Beta-blocker underutilization in our population may largely be explained by patients not filling a prescription they received at hospital discharge.

Conclusions

Data from this real-world observational study has increased our understanding of the impact of both prescriber and patient behavior on the implementation of MI secondary prevention guidelines in patients with T2DM. Additionally, as confounding is a major threat to validity in observational research, the predictors of β -blocker therapy identified in our study should be considered in the analysis of post-MI

clinical outcomes in patients with T2DM. Our study also confirmed the results from previous researchers that β -blockers were underutilized in this population when compared to the general post-MI population.

Clinical guidelines from the American Diabetes Association and the American Heart Association strongly recommend β -blocker therapy in patients with T2DM post-MI. Future research will be needed to determine whether these patients are not receiving this medication due to prescriber or patient behavior. The results from this study could assist in developing interventions targeted to patients less likely to receive this therapy.

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