Clinical Investigation

Low Utilization of Beta-Blockers Among Medicare Beneficiaries Hospitalized for Heart Failure With Reduced Ejection Fraction

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ABSTRACT

Background: The evidence-based beta-blockers carvedilol, bisoprolol, and metoprolol succinate reduce mortality and hospitalizations among patients with heart failure with reduced ejection fraction (HFrEF). Use of these medications is not well described in the general population of patients with HFrEF, especially among patients with potential contraindications.

Objectives: Our goal was to describe the patterns of prescription fills for carvedilol, bisoprolol, and metoprolol succinate among Medicare beneficiaries hospitalized for HFrEF, as well as to estimate the associations between specific contraindications for beta-blocker therapy and those patterns.

Methods and Results: With the use of the cohort of 15,205 Medicare beneficiaries hospitalized for HFrEF from 2007 to 2013 in the 5% Medicare random sample, we described prescription fills (30 days after discharge) and dosage patterns (1 year after discharge) for beta-blockers. By means of of Fine and Gray competing risk models, we estimated the associations between potential contraindications (hypotension, chronic obstructive pulmonary disease [COPD], asthma, and syncope) and prescription fill and dosing patterns while adjusting for demographics, comorbidities, and health care utilization. For beneficiaries who did not die or readmitted to the hospital, 38% of hospitalizations were followed by a prescription fill for an evidence-based beta-blocker within 30 days, 12% were followed by prescription fills for at least 50% of the recommended dose of an evidence-based beta-blocker within 1 year, and 9% were followed by a prescription fill for an up-titrated dose of an evidence-based beta-blocker within 1 year. The prevalence of the contraindications were 21% for hypotension, 48% for COPD, 15% for asthma, and 12% for syncope. Among beneficiaries who did not fill a prescription for an evidence-based beta-blocker within 30 days, 67% had at least 1 of these contraindications. Hypotension, COPD, and syncope were each associated with a ~10% lower risk of filling a prescription for an evidence-based beta-blocker.

Conclusions: Prescription fill and up-titration rates for evidence-based beta-blockers are low among Medicare beneficiaries with HFrEF, but contraindications explain only a minor part of these low rates. (*J Cardiac Fail 2019;25:343−351*)

Key Words: Medicare Part D, competing risks.

The American College of Cardiology Foundation and the American Heart Association recommend treating patients with heart failure with reduced ejection fraction (HFrEF) with the use of the evidence-based beta-blockers bisoprolol, carvedilol, and sustained-release metoprolol succinate[1] to reduce mortality and hospitalizations.[2−6] To avoid triggering

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decompensation, treatment should begin with a low dose and then be uptitrated over time.[1] A report from an HF registry study conducted from 2003 to 2004 that was designed to improve adherence to treatment guidelines found that 75% of patients hospitalized for HFrEF were discharged with a prescription for a beta-blocker, and 93% of those participants still had a prescription for a beta-blocker 60−90 days after discharge.[7] These data were based on a sample of hospitals that self-selected to enroll in a program to improve adherence to recommended treatment guidelines and did not account for prescriptions that were never filled. Research has shown that beta-blocker prescription rates in other populations, such as among patients eligible for both Medicare and Medicaid,[8] are much lower than in registry populations, potentially because of higher prevalences of contraindications, among other differences. Patients may not fill their prescriptions for beta-blockers due to potential side-effects, including hypotension, fatigue, atrioventricular block, and worsening HF.[1] Although 85% of patients in clinical trials for beta-blockers to treat HFrEF were able to tolerate the maximum dose after careful up-titration,[1] at most only 55% of older patients with HFrEF met the inclusion criteria for those trials, owing to potential contraindications, comorbidities, and age.[9]

Medicare Part D pharmacy data provide an opportunity to study a general sample of patients with HFrEF, using claims for beta-blocker prescription fills that include dose. In a cohort of Medicare beneficiaries hospitalized for HFrEF, we used Medicare Part D pharmacy claims data to describe 4 aspects of beta-blocker prescription fills: 1) filling a prescription for a beta-blocker within 30 days of hospital discharge; 2) filling a prescription for an evidence-based beta-blocker (carvedilol, bisoprolol, and sustained-release metoprolol succinate) within 30 days of hospital discharge; 3) filling a prescription for at least 50% of the target dose of an evidence-based beta-blocker within 1 year of hospital discharge; and 4) filling a prescription for an up-titrated dose of an evidence-based beta-blocker within 1 year of hospital discharge. We chose to include an analysis of evidence-based beta-blockers, given that these are the only beta-blockers with evidence from randomized controlled trials to reduce mortality and readmissions among patients with HFrEF. Other beta-blockers do not have as clear evidence for effectiveness in HFrEF.[1] Prescription fills for these particular beta-blockers indicate an intent to treat HF and not simply a comorbidity, such as hypertension. We also tested for associations between potential contraindications for beta-blocker therapy and the 4 outcomes to determine whether higher prevalence of contraindications in the Medicare population could explain potentially lower rates of beta-blocker use relative to clinical trial participants or HF registries.

Methods

Study Sample

We conducted a retrospective cohort study of Medicare beneficiaries hospitalized for HFrEF with the use of claims data. From a 5% random sample of Medicare beneficiaries, we identified episodes of hospitalization with a primary discharge diagnosis of HFrEF from 2007 to 2013, where the beneficiary was discharged alive. HFrEF was defined as an International Classification of Disease (9th edition; ICD-9) diagnosis code of 428.2x (systolic heart failure) or 428.4x (combined systolic and diastolic heart failure). In one study, 77% of patients with these diagnoses codes had confirmed HFrEF on medical record review.[10] Follow-up data were available through 2013. Beneficiaries were not included in the sample if they were not living in the US for the year before their HFrEF admission date, did not have continuous Medicare Part A, Part B, and Part D coverage for the year before HFrEF admission, were not in the Medicare 5% random sample for the year before HFrEF admission, or were 110 years of age or older on the HFrEF admission date. Beneficiaries with Medicare Advantage (Part C) were not included in this sample. We retained only the first hospitalization for HFrEF for each beneficiary during the study period.

Outcomes

Outcomes for this study were identified with the use of pharmacy claims for patient fills of beta-blocker prescriptions. As noted above, the 4 outcomes of interest in this study were: 1) filling a prescription for any beta-blocker within 30 days aftre HFrEF hospitalization discharge; 2) filling a prescription for an evidence-based beta-blocker within 30 days after HFrEF hospitalization discharge (ie, bisoprolol, carvedilol, or sustained-release metoprolol succinate); 3) filling a prescription for at least 50% of the recommended target dose of an evidence-based beta-blocker within 1 year after HFrEF hospitalization discharge; and 4) filling a prescription for an up-titrated dose of an evidence-based beta-blocker within 1 year after HF hospitalization discharge. The denominator for all outcomes was the entire cohort. For example, we measured the outcome of filling a prescription for at least 50% of the target dose among the entire cohort, not only those who had filled a prescription for an evidence-based beta-blocker. Target doses were defined in the American Heart Association/American College of Cardiology heart failure treatment guidelines.[1] Specifically, the daily target dosages were 10 mg once per day for bisoprolol, 50 mg twice per day for carvedilol, 80 mg once per day for controlled-release carvedilol, and 200 mg once per day for extended-release metoprolol. Each of the 4 outcomes was assessed independently from one another. For example, participants could reach at least 50% of the target dose of an evidence-based beta-blocker without uptitrating if their first prescription for a beta-blocker was for at least 50% of the target dose or if they started on a beta-blocker that was not evidence-based and then were switched to at least 50% of the target dose of an evidence-based beta-blocker. Participants were censored if follow-up time ended or a patient became ineligible for the study sample per the exclusion criteria described above (eg, Medicare

coverage lapsed). Recurrent hospitalizations and deaths were treated as competing risks.

Potential Contraindications for Beta-Blocker Therapy

We considered several potential contraindications for a beta-blocker prescription: hypotension, COPD, asthma, bradycardia, syncope, and atrioventricular block (first, second, or third degree). Detection of contraindications was based on ICD-9 diagnosis codes from combinations of inpatient, outpatient, skilled nursing facility (SNF), and home health agency claims. Because of the small number of hospitalizations with evidence of bradycardia (<2%) and atrioventricular block (<1%), we focused on hypotension, COPD, asthma, and syncope. Claims for contraindications were identified during the year before HFrEF hospitalization (see Supplementary Methods for definitions of these contraindications).

Other Variables

Potential confounders of the association between the contraindications and patterns of beta-blocker prescription fills were considered. Demographic variables included were age at HFrEF hospitalization admission, race (black, white, other), sex, Medicaid eligibility, Medicare Part D subsidies, region of residence, and nursing home residence. Comorbidities included were whether the beneficiary had coronary heart disease (CHD), stroke, hypertension, hyperlipidemia, diabetes, valvular heart disease, atrial fibrillation, other arrhythmias or conduction disorders, autoimmune or inflammatory disease, cancer, malnutrition, liver disease, anemia, or depression and was assessed during the year before hospitalization. We also included implantable cardiac device (cardiac resynchronization therapy−defibrillator, cardiac resynchronization therapy−pacemaker, defibrillator, pacemaker, or none), also assessed during the year before hospitalization. Indicators of health care utilization in the previous year (a hospitalization, an SNF stay, or filling a prescription for a beta-blocker before hospitalization [evidence-based beta-blocker, non−evidence-based beta-blocker, or no beta-blocker]) and length of stay during an HFrEF hospitalization were also considered as potential confounders.

Statistical Analysis

We calculated summary statistics of the potential confounders and 4 outcomes for the total sample, as well as by presence of each contraindication (hypotension, COPD, asthma, and syncope). Cumulative incidence functions were estimated for the 30-day and 1-year outcomes for the total cohort. Fine and Gray models[11] took into account the competing risks of hospitalization or death and were used to estimate hazard ratios (HRs) for the association between the contraindications with each of the beta-blocker outcomes. Given that the competing risks of hospitalization and death are common in this population, standard Cox regression models can not provide an unbiased estimate of the probability of filling a prescription by the specified follow-up time. Fine and Gray models allowed us to estimate the probability of filling a prescription, as well as HRs for filling a prescription based on the presence of a potential contraindication, among beneficiaries who did not die and were not hospitalized during the follow-up period.

Although we initially included beneficiaries with a discharge status code that indicated an SNF discharge in our main analysis, we conducted a sensitivity analysis excluding those beneficiaries, given that Medicare Part D does not cover prescription benefits during episodes of Medicare-covered SNF care. In addition to the sensitivity analysis that excluded those discharged to an SNF, we also conducted 3 other sensitivity analyses: one that excluded participants with bradycardia or atrioventricular block (any degree), one that performed stratified analyses by beta-blocker use during baseline, and one that excluded beneficiaries who had days of an evidence-based beta-blocker available on hospital admission according to previous prescription fills before admission. Finally, we conducted an analysis with the presence of any of the 4 contraindications as the exposure in a fully adjusted model to summarize the associations between each of the potential confounders and the beta-blocker prescription fill patterns. All analyses were conducted with the use of R and SAS (Cary, North Carolina) statistical software.

Results

After identifying the relevant sample of HF hospitalizations from the Medicare 5% random sample, our analysis sample consisted of 15,205 beneficiaries with a hospitalization for HFrEF (Supplemental Fig. 1). Most beneficiaries had previous hospitalizations for HF. Summaries of demographic variables, comorbidities, implanted cardiac devices, and health care utilization variables for the entire cohort, as well as for participants with each of the contraindications, are presented in Table 1.

Figure 1 shows the cumulative incidence functions for each outcome. Approximately 51% of the hospitalizations were followed with a claim for a prescription fill for a beta-blocker within 30 days, and even fewer of the hospitalizations were followed with a prescription fill for an evidence-based beta-blocker within 30 days. Twelve percent of hospitalizations were followed with a claim for a prescription filled for at least 50% of the target dose of an evidence-based beta-blocker within 1 year, and only 9% of hospitalizations were followed by up-titration of the dose of an evidence-based beta-blocker within 1 year.

Among the beneficiaries in the sample, 21% had hypotension, 48% had COPD, 15% had asthma, and 12% had syncope. Among beneficiaries who did not fill a prescription for an evidence-based beta-blocker within 30 days, 67% had ≥1 of these contraindications. Beneficiaries hospitalized with a contraindication were more likely to have had a diagnosis code of anemia and/or depression and to have been hospitalized for any cause during the previous year compared with the entire cohort. Beneficiaries with

Table 1. Summary Characteristics of Medicare Beneficiaries Hospitalized for Heart Failure With Reduced Ejection Fraction (HFrEF) From 2007 to 2013, Overall and in Subpopulations With Key Contraindications

Variable	Overall (n = 15,205)	Hypotension (n = 3,257)	COPD (n = 7,338)	Asthma (n = 2,341)	Syncope (n = 1,846)
Age at admission, y, mean ± SD	76.5 ± 12.1	76.5 ± 12.1	75.5 ± 11.6	74 ± 12.9	78.2 ± 11.5
Race					
Black	2184 (14)	387 (12)	945 (13)	422 (18)	254 (14)
Other	852 (6)	176 (5)	376 (5)	151 (6)	92 (5)
White	12,169 (80)	2694 (83)	6017 (82)	1768 (76)	1500 (81)
Women	7869 (52)	1593 (49)	3635 (50)	1373 (59)	911 (49)
Dual-eligible for Medicare and Medicaid	6146 (40)	1269 (39)	3279 (45)	1121 (48)	688 (37)
Medicare Part D subsidy	7291 (48)	1513 (46)	3838 (52)	1282 (55)	819 (44)
US Census region					
East North Central	2714 (18)	616 (19)	1334 (18)	427 (18)	331 (18)
East South Central	1498 (10)	296 (9)	781 (11)	199 (9)	172 (9)
Middle Atlantic	2265 (15)	460 (14)	1076 (15)	404 (17)	311 (17)
Mountain	579 (4)	125 (4)	284 (4)	95 (4)	67 (4)
New England	809 (5)	183 (6)	357 (5)	114 (5)	116 (6)
Pacific	1386 (9)	303 (9)	649 (9)	232 (10)	157 (9)
South Atlantic	2857 (19)	617 (19)	1381 (19)	427 (18)	363 (20)
West North Central	1195 (8)	262 (8)	553 (8)	165 (7)	133 (7)
West South Central	1902 (13)	395 (12)	923 (13)	278 (12)	196 (11)
Taking beta-blocker during baseline					
Evidence-based	7466 (49)	1782 (55)	3690 (50)	1152 (49)	1036 (56)
Other beta-blocker	3741 (25)	754 (23)	1735 (24)	534 (23)	417 (23)
None	3998 (26)	721 (22)	1913 (26)	655 (28)	393 (21)
Implanted cardiac device					
CRTD	1365 (9)	351 (11)	644 (9)	203 (9)	258 (14)
CRTP	75 (0)	14 (0)	36 (0)	13 (1)	17 (1)
Defibrillator	1323 (9)	374 (11)	653 (9)	212 (9)	195 (11)
Pacemaker	1565 (10)	381 (12)	702 (10)	231 (10)	305 (17)
None	10,877 (72)	2137 (66)	5303 (72)	1682 (72)	1071 (58)
Atrial fibrillation	7193 (47)	1763 (54)	3563 (49)	1085 (46)	980 (53)
Malnutrition	1252 (8)	450 (14)	725 (10)	202 (9)	195 (11)
Liver disease	710 (5)	209 (6)	361 (5)	125 (5)	90 (5)
Anemia	8548 (56)	2158 (66)	4324 (59)	1381 (59)	1192 (65)
Depression	3499 (23)	959 (29)	1963 (27)	708 (30)	533 (29)
Coronary heart disease	10,932 (72)	2600 (80)	5519 (75)	1697 (72)	1474 (80)
Stroke	888 (6)	271 (8)	452 (6)	143 (6)	189 (10)
Hypertension	12,337 (81)	2721 (84)	6102 (83)	1976 (84)	1617 (88)
Hyperlipidemia	6167 (41)	1558 (48)	3130 (43)	1020 (44)	889 (48)
Diabetes	7439 (49)	1532 (47)	3750 (51)	1269 (54)	895 (48)
Valvular or rheumatic heart disease	2242 (15)	606 (19)	1019 (14)	352 (15)	316 (17)
Other arrhythmia or conductive disorder	6058 (40)	1607 (49)	3041 (41)	1008 (43)	1039 (56)
Autoimmune or inflammatory disease	813 (5)	214 (7)	450 (6)	168 (7)	114 (6)
Cancer	3059 (20)	736 (23)	1495 (20)	475 (20)	412 (22)
Nursing home residence	2112 (14)	549 (17)	1151 (16)	329 (14)	306 (17)
Hospitalization during baseline	4354 (29)	1309 (40)	2448 (33)	849 (36)	735 (40)
Skilled nursing facility stay during baseline	2481 (16)	823 (25)	1441 (20)	449 (19)	468 (25)
Length of stay during HFrEF hospitalization, d, median (interquartile range)	5 (4−8)	6 (4−9)	5 (4−8)	5 (4−8)	5 (4−8)

Values are presented as n (%) unless otherwise specified. COPD, chronic obstructive pulmonary disease; CRTD, cardiac resynchronization therapy−defibrillator; CRTP, cardiac resynchronization therapy−pacemaker.

hypotension or syncope were more likely to have filled a prescription for an evidence-based beta-blocker during baseline or to have a defibrillator (with or without CRT) than the entire cohort. They were more likely to have had a diagnosis code for cardiovascular disease (CVD; CHD or stroke) in the previous year, and to have had hyperlipidemia or atrial fibrillation. Beneficiaries with COPD or asthma were more likely to be Medicaid eligible and to have a Medicare Part D subsidy. Beneficiaries with asthma tended to be younger, were more likely to be black and female, and were more likely to have had hypertension and diabetes in the year before hospitalization compared with the entire cohort. Overall, beneficiaries with hypotension or syncope appeared to have the highest overall burden of comorbidities, treatment with the use of beta-blockers or implantable cardiac devices, and risk factors for CVD compared with the entire cohort. Finally, beneficiaries with hypotension or syncope were more likely than the entire cohort to have had an SNF stay during the year before hospitalization.

Figure 2 shows the HRs and 95% confidence intervals (CIs) for each outcome and contraindication. Supplemental Table 1 contains the HRs and 95% CIs portrayed in Fig. 2. Beneficiaries with hypotension were less likely to fill a prescription for any beta-blocker within 30 days (HR 0.90, 95% CI 0.85−0.95), to fill a prescription for an evidence-based beta-blocker within 30 days (0.92, 0.87−0.99), and

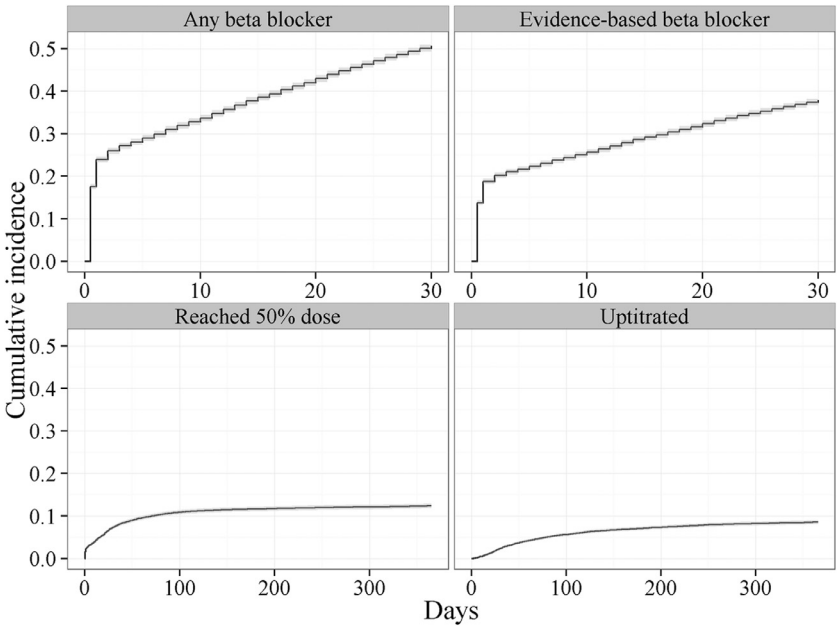

Fig. 1. Cumulative incidence functions for outcomes. Outcomes are receiving any beta-blocker within 30 days, receiving an evidence-based beta-blocker within 30 days, reaching at least 50% of the target dose of an evidence-based beta-blocker, and being up-titrated on an evidence-based beta-blocker within 1 year, given that the beneficiary has not died or been readmitted before the end of the follow-up period. Denominator for each panel is total cohort.

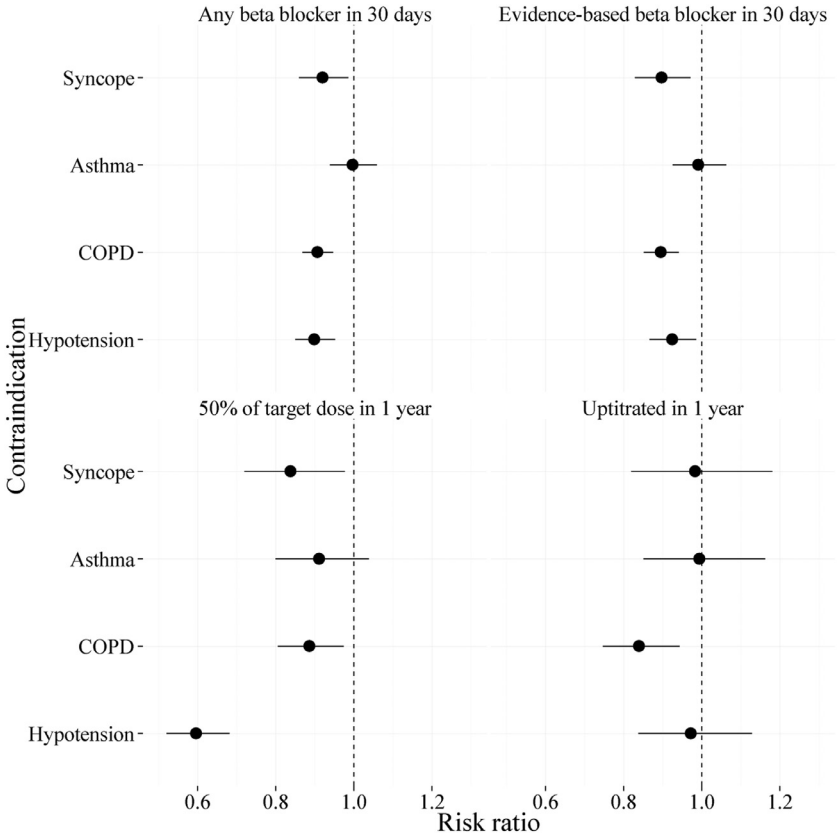

Fig. 2. Hazard/risk ratios (HR/RRs) for each contraindication for each outcome. Each competing risk model was adjusted for age, race, sex, region of residence, beta-blocker use during baseline, cardiac device, Medicaid eligibility on hospital admission, cost-sharing group, nursing home residence, coronary heart disease, stroke, hypertension, hyperlipidemia, diabetes, valvular or rheumatic heart disease, atrial fibrillation, other arrhythmia or conductive disorder, inflammatory or autoimmune disease, cancer, malnutrition, liver disease, anemia, depression, hospitalization, skilled nursing facility, and length of hospital stay during heart failure hospitalization. An HR/RR of 1 indicated no significant association. COPD, chronic obstructive pulmonary disease.

to receive at least 50% of the target dose of an evidence-based beta-blocker in 1 year (0.60, 0.52−0.68) and potentially less likely to be up-titrated within 1 year (0.97, 0.84−1.13) compared with those without hypotension. Compared with beneficiaries without COPD, beneficiaries with COPD had lower rates of filling a prescription for any beta-blocker within 30 days (HR 0.91, 95% CI 0.87−0.95) and for an evidence-based beta-blocker within 30 days (0.89, 0.81−0.97) compared with those without COPD. Beneficiaries with COPD were less likely to reach at least 50% of the target dose (0.90, 0.85−0.94) or to be up-titrated (0.84, 0.75−0.94) within 1 year compared with those without COPD. Beneficiaries with asthma did not have significantly lower risks of any of the outcomes compared with beneficiaries without asthma. Syncope was associated with a lower risk of filling a prescription for any beta-blocker within 30 days (HR 0.92, 95% CI 0.86−0.99) or an evidence-based beta-blocker within 30 days (0.90, 0.83−0.97), as well as a lower risk of filling a prescription for at least 50% of the target dose of an evidence-based beta-blocker within 1 year (0.84, 0.72−0.98). Syncope was not significantly association with filling a prescription for up-titrating an evidence-based beta-blocker within 1 year (0.98, 0.82−1.18).

The sensitivity analyses that either (1) excluded hospitalizations with claims for bradycardia or atrioventricular block (any degree) in the year before the HFrEF hospitalization, (2) excluded hospitalizations with discharge codes to an SNF, or (3) excluded beneficiaries who had days of an evidence-based beta-blocker available on hospital admission found only small changes in the HRs compared with the main analysis (Supplemental Figs. 2−4). However, associations between the potential contraindications and beta-blocker filling patterns were stronger among beneficiaries who did not use beta-blockers in the year before hospitalization compared with the associations among those who had filled beta-blocker prescriptions before hospitalization for HFrEF (Supplemental Fig. 5).

Supplemental Table 2 contains the HRs for a fully adjusted model when using the presence of any of the 4 contraindications as the exposure for each of the beta-blocker fill pattern outcomes. Women were more likely to fill a prescription for an up-titrated dose of an evidence-based beta-blocker within 1 year, and those with comorbidities tended to be less likely to do so. The best predictor of reaching at least 50% of the target dose of an evidence-based beta-blocker was having filled a prescription for an evidence-based beta-blocker during baseline (HR, 4.23, 95% CI 3.62−4.94).

Discussion

The purpose of the present study was to describe patterns of beta-blocker prescription fills in Medicare beneficiaries hospitalized for HFrEF, and to determine whether potential contraindications may explain those patterns. We found that fewer than half of hospitalizations were followed by a prescription fill for a beta-blocker specifically indicated in patients with HFrEF within 30 days. Approximately 1 in 10 hospitalizations for HFrEF were followed by reaching at least 50% of the target dose of an evidence-based beta-blocker or by up-titration of an evidence-based beta-blocker within 1 year of hospital discharge. Patients with a potential contraindication were only slightly less likely to fill a prescription for an evidence-based beta-blocker, or to fill prescriptions for guideline-concordant doses of these beta-blockers over time. Prescription fill patterns among the Medicare population, in which comorbidities are common, may differ from the subpopulation of patients that were eligible for the randomized controlled trials for bisoprolol, carvedilol, and sustained-release metoprolol succinate.

These results supplement findings from HF registries to provide an understanding of whether patients with HFrEF are generally treated with beta-blockers according to national guidelines. Three-fourths of the patients in the OPTIMIZE-HF registry with HFrEF had a prescription for a beta-blocker at discharge, and more than 90% of them still had the prescription in 60−90 days.[7] However, for those on carvedilol, only one-third ever had the dose of their beta-blocker adjusted within that time frame.[12] This discrepancy between our results and the results from OPTIMIZE-HF could occur because registries tend to consist of hospitals that are attempting to improve patient care (eg, improving beta-blocker prescription rates). Bertoni et al[8] found that among a sample of Medicare and Medicaid beneficiaries in North Carolina with HFrEF, only 48% of beneficiaries had a prescription for a beta-blocker, and only 12% had a contraindication, indicating that 40% of patients might have been eligible for treatment with a beta-blocker. Another explanation for the discrepancy between estimates of prescription rates and fill rates is that not all patients with HFrEF who are prescribed a beta-blocker actually fill the prescription. Prescription fills are likely a better indicator of patient behavior than discharge prescription rates, which might be a better representation of provider behavior than patient behavior. Prescription rates for beta-blockers at hospital discharge are a recommended performance measure for quality of care,[13] but the low prescription fill rates among Medicare beneficiaries compared with prescription rates in national registries suggests that prescription fill rates might be an additional factor to consider when measuring quality of care. Finally, the results of our analysis stratified by beta-blocker use preceding the hospitalization, showing that contraindications tended to be relevant only when the beneficiary was not using beta-blockers before hospitalization, corroborate findings from the Get With the Guidelines—Heart Failure registry, which found that the best predictor for discharge prescription for an evidence-based beta-blocker is being admitted with a prescription for an evidence-based beta-blocker.[14] Further investigation of the causes of discrepancies between prescription rates and prescription fill rates for beta-blockers among patients with HFrEF is warranted.

A recent study[15] using the same definition of HFrEF and Part D claims for the same beta-blockers among

beneficiaries discharged to an SNF estimated slightly higher prescription fill rates at 90 days (53%) than we observed at 30 days (35%−40%). Most beneficiaries who filled a prescription for a beta-blocker filled it shortly after discharge, suggesting that the difference in length of follow up between the 2 studies does not fully account for the difference in estimated probabilities of filling a prescription. Although our study and the one by Li et al had identical methods of identifying beneficiaries with HFrEF and identifying prescription fills for evidence-based beta-blockers, there were differences that might explain the lower estimated probabilities in our study, including Li et al's focus on a beneficiary population that might have increased health care utilization compared with the entire population of beneficiaries with HFrEF[16] and exclusion of participants who died within the 90-day follow-up period. Therefore, the estimated probabilities of filling a prescription from the study by Li et al apply to beneficiaries discharged to an SNF who survived to 90 days after hospitalization, whereas our estimated probabilities apply to a larger group of beneficiaries with multiple discharge types.

Even though 85% of patients with HFrEF in clinical trials of beta-blockers are able to tolerate the target recommended dose, only about one-fourth of Medicare beneficiaries with HFrEF and at most one-half of those with HFrEF would have met the inclusion criteria for those clinical trials.[9] Few Medicare beneficiaries in the present study filled prescriptions that were at least 50% of the target dose or filled prescriptions that were up-titrated, which is the pattern of care recommended by national guidelines.[1] Previous studies suggest that the likelihood of reaching the target dose of a beta-blocker among patients with HFrEF increased from 1999 to 2004,[17] but we do not know whether that trend has continued. There are potentially compelling clinical reasons not to prescribe or up-titrate a beta-blocker for a patient with HFrEF, including patient preferences, limited expected lifespan, frailty, and intolerable side-effects or medication interactions during previous regimens of the medications, none of which could be assessed in the present study.[18] The potential impact of these factors on evidence-based beta-blocker prescription fill patterns among patients with HFrEF should be investigated.

The present study has potential implications for reimbursement policies and management guidelines. Reducing hospital readmissions for beneficiaries with HFrEF can both reduce costs to the Centers for Medicare and Medicaid Services (CMS) and improve beneficiary outcomes, and carvedilol, bisoprolol, and sustained-release metoprolol succinate have been shown to reduce readmissions in this population. However, our findings suggest that a subset of Medicare beneficiaries with HFrEF who could benefit from taking these beta-blockers are not filling prescriptions for them, given the modest associations between potential contraindications and prescription fill patterns. Therefore, reimbursement policies by CMS that better encourage integrated inpatient and outpatient management to support use of evidence-based beta-blockers among beneficiaries with HFrEF have the potential to reduce their lifetime costs of care by reducing hospital readmissions. Primary care physicians, who are responsible for much of the medical management of patients with HF, report that hypotension and other treatment effects are major barriers to use and up-titration of beta-blockers.[19] This finding suggests that increasing use of these medications may require development of protocols for their use that are safe and practical for use in primary care settings among patients with multiple comorbidities, including potential contraindications.

Study Limitations and Strengths

The results of our study must be interpreted in light of its limitations. Medicare claims do not include measures of ejection fraction, so we relied on diagnosis codes for HF with systolic dysfunction. Previous studies have shown a 77% predictive value of using claims-based definitions to identify those with HFrEF,[10] indicating that the majority of beneficiaries in our study had HFrEF. Approximately 30% of Medicare beneficiaries are not enrolled in a Medicare Part D prescription drug plan (eg, veterans or those paying out-of-pocket).[20] These individuals were not included in our study, potentially limiting generalizability. We also could not assess the relationship between other important contraindications, such as bradycardia or atrioventricular block, and likelihood of filling a prescription, owing to a low prevalence of these conditions in our study sample (2%). None of the conditions that we examined are absolute contraindications to beta-blockers. Medicare claims do not have direct measures of contraindications or indicators of contraindication severity, preventing us from determining whether contraindications with severe symptoms had stronger associations with beta-blocker prescriptions fills than we found in our study. We did not investigate potential causes for low prescription fill rates for beta-blockers beyond presence of contraindications. Our findings can not generalize to the population of beneficiaries on Medicare Advantage ("Part C"), because claims for those participants are not included in Medicare claims data available for research. Finally, we could not determine discharge prescription status for study participants, because this information is not available in claims data. Even among Medicare Part D beneficiaries discharged with a prescription for a beta-blocker, medication adherence to beta-blockers is ∼60%.[21]

Study strengths include the use of actual prescription fills for beta-blockers instead of only receipt of prescription, and the use of a large, generalizable, population-based cohort. Competing risk survival models were used to account for the competing events of hospitalization and death, which allowed us to provide unbiased estimates for the subpopulation of patients most likely to benefit from interventions that could increase adherence to beta-blockers.

Conclusions

Among a cohort of Medicare beneficiaries hospitalized for HFrEF, we found that fewer than 40% of the hospitalizations

were followed by a prescription fill for carvedilol, bisoprolol, or metoprolol succinate within 30 days, given that the beneficiary did not die or was not readmitted within 30 days. After adjusting for whether the beneficiary was taking any beta-blocker before the hospitalization, demographics, comorbidities, and length of stay in the hospital, beneficiaries with hypotension, COPD, or syncope were ~10% less likely to fill a prescription for these beta-blockers within 30 days. Contraindications had similar modest or null associations with reaching at least 50% of the target dose or up-titrating, with the exception of those with hypotension having a 40% lower risk of reaching at least 50% of the target dose. Although there are compelling reasons to avoid beta-blocker therapy in patients with HFrEF that may not be readily assessed in administrative data, our findings suggest that there are Medicare beneficiaries with HFrEF who may have lower risk of mortality and readmission with closer adherence to national treatment guidelines.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cardfail.2018.10.005.

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