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Medication Initiation Burden Required to Comply with Heart Failure Guideline Recommendations and Hospital Quality Measures

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Abstract

Background—Guidelines for heart failure (HF) recommend prescription of guideline-directed medical therapy before hospital discharge; some of these therapies are included in publicly reported performance measures. The burden of new medications for individual patients has not been described.

Methods and Results—Get With The Guidelines-HF registry 2008–2013 collected prescribing, indications, and contraindications for angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ACEI/ARB), beta-blockers (BB), aldosterone antagonists (AldA), hydralazine/isosorbide dinitrate (H/ISDN), and anticoagulants. The difference between a patient's

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medication regimen at hospital admission and that recommended by HF quality measures at discharge was calculated. Among 158,922 patients from 271 hospitals with a primary discharge diagnosis of HF, initiation of ACEI/ARB was indicated in 18.1% of all patients (55.5% of those eligible at discharge were not receiving ACEI/ARB at admission), BB in 20.3% (50.5% of eligible), AldA in 24.1% (87.4% of eligible), H/ISDN in 8.6% (93.1% of eligible), and anticoagulant in 18.0% (58.0% of eligible). Cumulatively, 0.4% of patients were eligible for 5 new medication groups, 4.1% for 4, 9.4% for 3, 10.1% for 2, and 22.7% for 1; 15.0% were not eligible for new medications because of adequate prescribing at admission; and 38.4% were not eligible for any medications recommended by HF quality measures. Compared with newly indicated medications (mean 1.45±1.23), actual new prescriptions were lower (mean 1.16±1.00).

Conclusions—A quarter of patients hospitalized with HF need to start more than 1 medication to meet HF quality measures. Systems for addressing medication initiation and managing polypharmacy are central to HF transitional care.

Keywords

Heart Failure; Quality of Health Care; Prescribing Patterns; Physician; Medication Therapy Management; Medication Adherence

INTRODUCTION

Initiation and continuation of individual guideline-directed medical therapies prior to hospital discharge has been associated with improved adherence and clinical outcomes for patients with heart failure (HF).[1–3] Reflective of these data, current clinical practice guidelines and hospital quality measures for HF include the following medications at discharge: 1) angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) for HF with reduced ejection fraction (HF*r*EF), 2) beta-blocker (BB) for HF*r*EF, 3) aldosterone antagonists (AldA) for HF*r*EF, 4) hydralazine with isosorbide dinitrate (H/ISDN) for HF*r*EF among African-American patients, and 5) anticoagulants for those with atrial fibrillation.[4,5] Quality measures are increasingly tied to hospital recognition, public reporting, and payments.[6]

The vast majority of evidence for HF-related medical therapy derives from serial studies in which single medications were added to stable existing medical regimens, typically in an order dictated by scientific discovery rather than practical or physiological considerations. In the process of compiling this fragmented evidence, guidelines and quality measures in effect recommend that all of these medications be prescribed by the time of hospital discharge. The actual number of new medications recommended for individual patients at the time of hospital discharge by these comprehensive HF guidelines has not been well described. Given challenges around medication access and adherence,[7] which can be compounded by new and increasing numbers of medications at the difficult time of hospital-to-home transitions,[8] understanding the cumulative burden posed by guidelines and quality measures should help providers and health systems triage appropriate energy towards addressing newly recommended medications. Additionally, finding that current guidelines recommend for the simultaneous start of multiple medications in large numbers of patients would also fuel the need for research into optimal timing and sequencing for such initiation. Therefore, we set

out to quantify the difference between the actual medication regimen at the time of admission and the recommended medication regimen at the time of discharge according to HF guidelines and quality measures, after accounting for documented contraindications/intolerance to such therapy.

METHODS

Data Source

We conducted a cross-sectional study using data from the Get With The Guidelines®–Heart Failure (GWTG-HF) voluntary quality improvement initiative. The design and validity of this program's methods and data capture have been published previously.[9–11] Briefly, trained personnel at each site abstract clinical data for all patients admitted with HF in compliance with The Joint Commission and Centers for Medicare and Medicaid Services standards for quality indicators. Variables collected include demographic and clinical characteristics, medical history, medications, in-hospital treatments, in-hospital outcomes, and discharge disposition. Quintiles is the data collection coordination center for the American Heart Association/American Stroke Association GWTG programs. Their Internet-based Patient Management Tool performs checks to ensure the completeness of the reported data. Additionally, data quality is monitored independently and reports are generated to confirm the completeness and accuracy of submitted data. Hospital data elements are collected for all enrolling hospitals from the American Hospital Association database. Patient data are de-identified in accordance with the Health Insurance Portability and Accountability Act and a random hospital identifier is used to identify the various hospitals. All participating institutions were required to comply with local regulatory and privacy guidelines and to secure institutional review board approval. Because data are used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the common rule. The Duke Clinical Research Institute (Durham, North Carolina) serves as the data analysis center and has an agreement to analyze the aggregate de-identified data for research purposes.

Patients and Hospitals

We confined the current analysis to hospital admissions between April 1, 2008 and June 30, 2013 at hospitals fully participating in the GWTG-HF program. Fully participating hospitals were considered to be those with no more than 25% of history panel forms incomplete. We then excluded the following patients: those with inter-hospital transfer; those with documentation of comfort measures only; those with discharge destination missing, undetermined, hospice, or left against medical advice; and those who died in hospital.

Subgroups of interest were defined a priori. Prior history of HF was defined as medical history of HF or prior hospitalization for HF. Ischemic heart disease as the etiology for HF was defined as a medical history of coronary artery disease or myocardial infarction, or prior percutaneous coronary intervention or coronary artery bypass grafting. HF*r*EF was defined as most recent quantitative left ventricular ejection fraction (LVEF) <40% or qualitative LVEF moderately or severely reduced.

Medication Quality Measures

The GWTG-HF data collection form includes detailed capture of admission medications, documentation of LVEF, discharge medications, and contraindications to evidence-based therapies. Medication quality metrics defined by GWTG-HF during the study period were the following: 1) ACEI or ARB for LVEF <40%, 2) BB for LVEF <40%, 3) AldA for LVEF <35%, 4) H/ISDN for LVEF <40% among African-American patients, and 5) anticoagulants for those with atrial fibrillation. If quantitative LVEF was missing, qualitative moderate or severe reduction in LVEF replaced the reduced LVEF cutoffs. Contraindications and intolerances must be selected from a drop-down list of approved reasons. For example, contraindications to AldA include serum potassium >5 mmol, serum creatinine >2.5 mg/dL in men and >2.0 mg/dL in women, and history of dialysis. A complete list of HF Achievement Measures and Quality measures can be found online at http://www.heart.org/idc/groups/heart-public/@wcm/@private/@hcm/@gwtg/documents/downloadable/ucm_310967.pdf. Details of performance measures for Advanced Certification HF are at http://www.jointcommission.org/assets/1/6/2014_ACHF_Manual_6_required_measures.pdf.

Statistical Analysis

We calculated the difference between the patient's medication regimen at the time of admission and what would be recommended by current guidelines and quality measures at the time of discharge, as well as the number of new HF medications actually prescribed at discharge. Patient and hospital-level characteristics were selected based upon previous literature and clinical criteria.[12] Percentages and medians (25^{th}, 75^{th} percentiles) were reported to describe the distribution of categorical and continuous variables. Chi-square and Wilcoxon two-sample tests were used to compare characteristics between patients who had 2 or fewer new medications and those who had 3 to 5 new medications to initiate at discharge.

Multivariable logistic regression was used to identify factors associated with increased or decreased odds of a patient getting a recommended medication prescribed at discharge among the patients who were eligible and not treated prior to discharge. Among the 5 potential options, each medication class was considered as an opportunity such that a patient could have as many as 5 responses or as few as one response: one for each newly recommended medication. The generalized estimating equation method using exchangeable working correlation structure was used to account for correlation within patients when patients had more than one newly recommended medication. The model was also adjusted by the newly recommended medication profile (to account for differences in patient eligibility) and by the medication to which each observation applies (to account for differences in average prescribing rate for each of the medications). Patient-level variables included demographics (age, gender, race [Black, Hispanic ethnicity, other race, and White]), medical history (COPD, diabetes, hyperlipidemia, hypertension, PVD, CVA/TIA, ICD, anemia, pacemaker, dialysis chronic, renal insufficiency, depression, ischemic heart disease, smoking, prevalent heart failure, and atrial fibrillation/flutter), insurance status (Medicare, Medicaid, private/other, none), and vital signs (heart rate, systolic blood pressure at admission). Patients with gender missing were excluded. Other categorical variables with missing observations (all <5% missing) were imputed to the most common category. Body

mass index and laboratory values at admission had more than 20% missing so were not included in modeling. Other continuous variables with missing observations were imputed to the medians. A p value ≤0.05 was considered statistically significant for all tests. All analyses were performed with SAS software version 9.2 (SAS Institute, Cary, NC).

RESULTS

Hospital and Patient Characteristics

The final study sample included 158,922 patients from 271 hospitals discharged between April 1, 2008 and June 30, 2013. Among the patients eligible for at least one new medication, median age was 73 years, 60% were Caucasian, comorbidities were present in the majority of patients, and median length of stay was 4 days (Table 1). The majority of hospitals were academic, though few performed heart transplants.

Recommended Medication Initiation Burden

ACEI/ARB initiation was indicated in 18.1% of all patients (55.5% of those eligible at discharge were not receiving ACEI/ARB at admission), BB in 20.3% (50.5% of eligible), AldA in 24.1% (87.4% of eligible), H/ISDN in 8.6% (93.1% of eligible), and anticoagulant in 18.0% (58.0% of eligible) (Table 2). Cumulatively, 13.9% of patients were eligible for 3 to 5 new medication groups, and 32.8% were eligible for 1 to 2 new medication groups; whereas 15.0% were not eligible for any new medications because of adequate prescribing prior to admission, and 38.4% were not eligible for any medications recommended by HF quality measures (99.0% of whom did not have reduced LVEF) (Table 3). The number of patients prescribed a medication at admission and discharged without the prescription was small, ranging from 0.68% for BB to 1.58% for anticoagulants.

Common Combinations of Newly Recommended and Prescribed Medications

The 5 most common combinations of newly recommended medications at discharge were anticoagulant only (23.5%), ACE/ARB+BB+AldA (12.0%), AldA only (6.1%), ACE/ARB +BB+AldA+H/ISDN (4.6%), and ACE/ARB+BB (4.4%). The combinations of medications that were newly prescribed paralleled the recommendations, albeit at lower frequencies.

New Medication Recommendations by Patient Subgroups

Among patients who were eligible for at least one new medication at discharge (N=97,888), 21.4% had no prior diagnosis of HF, 69.8% had LVEF <40%, and 55.6% had an ischemic etiology for HF. Patients without a prior HF diagnosis had a higher number of recommended medications to initiate compared with those with a prior HF diagnosis (mean 1.7±1.3 versus 1.3±1.2). Patients with LVEF <40% had a higher number of recommended medications to start compared to those with LVEF ≥40% (mean 1.8±1.3 versus 0.6±0.5). Patients without a history of ischemic heart disease had a higher number of newly recommended medications to start compared to those with ischemic heart disease (mean 1.56±1.27 versus 1.29±1.16).

Prescribing of Newly Recommended Medications

Compared with the number of new medications indicated (mean 1.45±1.23), the number of actual new prescriptions at discharge was lower (mean 1.16±1.00). ACEI/ARB was prescribed in 91.2% of those eligible but not receiving it prior to admission, BB prescribed in 94.1%, AldA in 27.2%, H/ISDN in 18.9%, and anticoagulant in 56.4%. In multivariable analysis, a prescription at discharge for the newly recommended medications was associated with the following patient characteristics: younger age, male, Caucasian, Medicare and non-Medicaid insured; history of hyperlipidemia, implantable cardioverter-defibrillator, or renal insufficiency; absent history of PVD, anemia, pacemaker, dialysis, depression, ischemic heart disease, and smoking; absence of reduced LVEF; and higher heart rate (Table 4).

DISCUSSION

Among patients hospitalized with HF, 47% needed to start at least one new HF-related medication by discharge, 24% needed to start more than one, and 14% needed to start 3 or more in order to be in compliance with current HF guidelines and quality measures. These numbers do not include additional medications indicated for non-HF comorbidities. This provides the first large description of how layering evidence-based guideline recommendations can cumulatively lead to a high number of newly recommended medications for patients discharged after worsening HF. Other studies, including analyses from GWTG-HF, have assessed overall indications for and prescribing of HF medications but have not distinguished between pre-existing and new use of these medications nor have they provided an assessment of total medication initiation burden.[13,14] As quality measures are increasingly used in public reporting and payment decisions,[6] evaluation of the cumulative burden created by process measures is crucial. While discrete recommendations may make sense in isolation, the simultaneous effect of multiple measures on patient well-being and care delivery should be factored into the overall design of reform efforts.

Research into the relative benefit of mass initiation of medications prior to discharge versus sequential initiation that extends into the ambulatory setting is needed. Staged medication initiation could be less overwhelming to patients in the difficult transition period and reduce the risk of hypotension and other side effects. Additionally, simultaneous addition of ACEI/ARB and AldA, which both have effects on kidney function and potassium handling, has not been well studied; fears of renal dysfunction and hyperkalemia may explain some of the underuse of AldA. However, these concerns must be balanced against research showing that inpatient initiation of individual medications is relatively safe and leads to higher use of these life-prolonging medications in the long-term.[3,15,16] With current recommendations for 1-week post-discharge follow-up and increased attention on the transitional care period, the opportunity for sequential addition of medications exists[4,17] If staged initiation is considered to be preferable, the order in which these medications should be started in various populations is relatively unknown and also deserves further research.

As expected from the linkage between reduced LVEF and indications for many neurohormonal-antagonist therapies, patients with HF*r*EF had a relatively higher burden of recommended medications to initiate compared to patients with preserved LVEF. With the common co-occurrence of HF and atrial fibrillation, HF medications and anticoagulation

were also frequently co-recommended. Thus, certain patient populations, including those with multi-morbidity, are likely to be disproportionately affected by this layering of guideline recommendations and quality measures, and may warrant special attention.

Medication adherence research has focused primarily on continuation of medications; however, additions to medication regimens are typically more challenging for patients.[18] Rates of primary nonadherence (i.e. never filling a medication) often exceed the rate of medication discontinuation.[19,20] Thus, optimizing the process for getting patients onto medications in the first place may be one of the most critical aspects of adherence interventions.[21–23] Therefore, transitional care systems that help ensure patients actually pick up and correctly start newly prescribed medications are likely to provide high value.[24] Medication initiation strategies should be complemented by efforts to limit potential burdens and side effects. These necessarily complex medication regimens, particularly for HF*r*EF and multi-morbidity, demand multifaceted disease-management solutions that are yet-to-be perfected.[25]

The study has several limitations. Hospitals voluntarily participating fully in GWTG-HF may not be representative of hospitals or HF patients in the United States; however, prior study has shown that patients in GWTG-HF are relatively similar to cross-sectional samples of national HF hospitalizations.[10] Data were collected by chart review and so depend on the accuracy and completeness of documentation, particularly in terms of contraindications and intolerance. GWTG-HF collects data by site and hospitalization event, not by unique patients, such that the effect of recurrent hospitalizations for individual patients is not specifically accounted for in this analysis. Laboratory values are optional fields in GWTG-HF with a high rate of missingness, to an extent that we decided not to impute laboratory values or confine the analysis to patients with complete laboratory values; however, sites were required to choose contraindications to medications from a menu of accepted reasons that included hyperkalemia and worsening renal function for ACEI/ARB and AldA, such that these variables do get incorporated into data capture. We do not have data on post-discharge adherence or outcomes that would have allowed for further investigation into the potential implications of multiple medication starts. Additionally, this analysis does not account for non-HF medications, which may significantly alter the complexity of discharge medication changes as narrowly reported here.

Conclusions

Nearly half of patients hospitalized with HF need to start at least one new medication, with 24% having indications for at least 2 medications and 14% for 3 or more medications, in order to comply with current HF guidelines and hospital quality measures. Systems for addressing medication initiation and managing polypharmacy are central to HF transitional care efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Patient and hospital characteristics for patients hospitalized with heart failure, overall and stratified by number of medications that guidelines recommend for initiation

Median (25th, 75th) or percent	Total	Not Eligible for Any HF Medications	Receiving All Indicated Medications at Admission	New Medications Recommended*		P-value
	N=158,922	N=61,034	N=23,792	1–2 Meds N=52,171	3–5 Meds N=21,925	
Patient Characteristics						
Age, years	75 (63, 84)	75 (63, 85)	77 (66, 84)	75 (64, 84)	67 (55, 79)	<0.0001
Female	48.3%	58.2%	46.4%	43.3%	34.7%	<0.0001
Black	18.8%	18.0%	8.0%	17.7%	35.5%	<0.0001
Medicare insured	60.2%	61.8%	61.0%	62.3%	49.4%	<0.0001
Atrial fibrillation, chronic	35.1%	12.7%	64.2%	47.8%	31.3%	<0.0001
COPD or asthma	31.4%	33.4%	33.7%	30.6%	25.3%	<0.0001
Diabetes	44.1%	49.1%	45.1%	41.8%	34.6%	<0.0001
Hyperlipidemia	49.7%	49.6%	56.0%	50.7%	40.0%	<0.0001
Hypertension	78.5%	82.1%	79.9%	77.3%	69.8%	<0.0001
Peripheral vascular disease	12.2%	12.6%	14.2%	12.4%	8.0%	<0.0001
CVA or TIA	15.1%	15.0%	17.7%	15.1%	11.9%	<0.0001
Anemia	20.0%	24.4%	20.6%	18.4%	11.2%	<0.0001
Dialysis, chronic	4.1%	6.3%	3.6%	3.1%	1.0%	<0.0001
Renal insufficiency	22.8%	26.0%	23.8%	22.1%	14.2%	<0.0001
Depression	10.7%	11.9%	12.1%	10.0%	7.5%	<0.0001
Smoking	16.5%	15.1%	12.1%	16.2%	25.7%	<0.0001
Prevalent heart failure	69.8%	64.0%	78.6%	73.8%	65.3%	<0.0001
Valvular heart disease	17.7%	15.4%	24.6%	18.9%	13.0%	<0.0001
ICD	10.3%	2.7%	13.6%	14.8%	16.9%	<0.0001
LVEF <40% or moderately to severely reduced	43.4%	1.2%	48.1%	67.0%	100%	<0.0001
BMI, kg/m2	28.1 (23.7, 34.2)	29.2 (24.2, 36.2)	27.8 (23.7, 33.5)	27.3 (23.4, 32.8)	27.7 (23.5, 33.4)	<0.0001
Heart rate, bpm	82 (70, 97)	80 (69, 93)	80 (70, 94)	84 (71, 99)	91 (77, 106)	<0.0001
Systolic blood pressure, mmHg	140 (121, 161)	148 (128, 172)	135 (117, 154)	135 (117, 155)	136 (118, 156)	<0.0001
Length of stay, days	4 (3, 6)	4 (3, 6)	4 (3, 6)	4 (3, 7)	4 (3, 6)	<0.0001

Median (25th, 75th) or percent	Total	Not Eligible for Any HF Medications	Receiving All Indicated Medications at Admission	New Medications Recommended*		P-value
	N=158,922	N=61,034	N=23,792	1–2 Meds N=52,171	3–5 Meds N=21,925	
Hospital Characteristics						
Number of beds	400 (270, 601)	394 (258, 593)	410 (250, 610)	405 (280, 601)	404 (300, 593)	<0.0001
Academic status	66.5%	63.6%	64.3%	68.3%	72.6%	<0.0001
Heart transplants performed	8.8%	7.1%	10.4%	9.9%	9.3%	<0.0001

HF indicates heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; TIA, transient ischemic attack; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; and BMI, body mass index.

*The population for the multivariable analysis used the patients with new medication recommended (N=74096).

Table 2

Eligibility, baseline use at admission, recommended new prescriptions, prescription at discharge, and actual increase for individual medication

Medication	Eligible, n (of all patients, %)	Use prior to admission, n (of eligible patients, %)	Newly recommended, n (of eligible patients, %)	Total Prescribed at discharge*, n (of eligible patients, %)	Newly prescribed at discharge, n (of newly recommended for patients, %)
ACEI/ARB	51,847 (32.62)	23,059 (44.48)	28,788 (55.52)	48,842 (94.20)	26,257 (91.21)
βB	63,878 (40.19)	31,595 (49.46)	32,283 (50.54)	61,532 (96.33)	30370 (94.07)
Aldosterone antagonist	43,780 (27.55)	5,532 (12.64)	38,248 (87.36)	15,353 (35.07)	10400 (27.19)
H/ISDN	14,742 (9.28)	1,015 (6.89)	13,727 (93.11)	3,480 (23.61)	2596 (18.91)
Warfarin	49,304 (31.02)	20,709 (42.00)	28,595 (58.00)	36,061 (73.14)	16133 (56.42)

ACEI/ARB indicates angiotensin converting enzyme inhibitors/angiotensin receptor blockers; βB, beta-blockers; and H/ISDN, hydralazine/isosorbide dinitrate.

*Includes continuing prescription (with use prior to admission) and newly prescribed.

Table 3

Cumulative number of medications patients were to initiate based on heart failure measures, overall and by left ventricular ejection fraction

Number of Medications Patient Eligible to Initiate	All Patients*		LVEF <40% or moderate to severe dysfunction		LVEF >=40% or normal to mild dysfunction	
	Number of Patients	Percent of All Patients	Number of Patients	Percent of Patients	Number of Patients	Percent of Patients
5	566	0.4%	566	0.8%		
4	6,496	4.1%	6,496	9.4%		
3	14,863	9.4%	14,863	21.5%		
2	16,067	10.1%	16,067	23.3%		
1	36,104	22.7%	18,884	27.4%	16,691	19.3%
0	84,826	53.3%	12,157	17.6%	69,761	80.7%

*All patients include the 2% of the cohort with missing LVEF/systolic function.

Table 4

Multivariable model for factors associated with prescribed medication among the newly recommended medications from admission to discharge

Variable	OR (95% CI)	P-value
Age (per 10 years)	0.82 (0.81, 0.83)	<0.0001
Female (vs. male)	0.96 (0.93, 0.99)	0.0039
Race: Black (vs. White)	0.90 (0.83, 0.99)	0.022
Hispanic ethnicity (vs. Not)	0.78 (0.74, 0.83)	<0.0001
Race: Other (vs. White)	0.79 (0.75, 0.83)	<0.0001
Insurance: None (vs. private/HMO/other insurance)	1.01 (0.94, 1.08)	0.87
Insurance: Medicaid (vs. private/HMO/other insurance)	0.87 (0.82, 0.92)	<0.0001
Insurance: Medicare (vs. private/HMO/other insurance)	1.11 (1.07, 1.15)	<0.0001
PMHX: Pulmonary	0.97 (0.93, 1.00)	0.055
PMHX: Diabetes	1.01 (0.98, 1.04)	0.48
PMHX: Hyperlipidemia	1.14 (1.10, 1.17)	<0.0001
PMHX: Hypertension	1.01 (0.98, 1.05)	0.50
PMHX: PVD	0.93 (0.89, 0.98)	0.0074
PMHX: CVA/TIA	1.03 (0.99, 1.08)	0.14
PMHX: ICD	1.09 (1.04, 1.14)	0.0003
PMHX: Anemia	0.95 (0.91, 0.99)	0.023
PMHX: Pacemaker	0.94 (0.90, 0.98)	0.0084
PMHX: Dialysis Chronic	0.51 (0.46, 0.57)	<0.0001
PMHX: Renal insufficiency	1.08 (1.04, 1.13)	0.0002
PMHX: Depression	0.89 (0.85, 0.94)	0.0001
PMHX: Smoker	0.95 (0.91, 0.99)	0.012
Prior HF history (vs. new HF)	1.01 (0.98, 1.05)	0.48
LVSD (vs. not)	0.51 (0.46, 0.56)	<0.0001
Atrial fib, chronic/recur history or during this hospitalization	0.97 (0.91, 1.03)	0.27
Systolic BP at admission (per 10 units)	1.00 (0.99, 1.00)	0.22
Heart rate at admission (per 10 units)	1.03 (1.02, 1.04)	<0.0001

OR indicates odds ratio; CI, confidence interval; HMO indicates health maintenance organization; PMHX, patient medical history; PVD, peripheral vascular disease; CVA, cerebrovascular accident; TIA, transient ischemic attack; ICD, implantable cardioverter-defibrillator; HF, heart failure; LVSD, left ventricular systolic dysfunction; and BP, blood pressure.