Treatment Initiation Patterns, Modifications, and Medication Adherence Among Newly Diagnosed Heart Failure Patients: A Retrospective Claims Database Analysis

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ABSTRACT

BACKGROUND: Heart failure (HF) is a debilitating disease associated with high mortality and frequent hospitalizations. American College of Cardiology Foundation and American Heart Association (ACCF/AHA) guidelines recommend the following drug classes for HF treatment: angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor II blocker (ARB) for patients intolerant to ACEI, beta blocker (BB), and aldosterone antagonist (AA).

OBJECTIVE: To examine, in a real-world setting, the treatment initiation pattern among newly diagnosed HF patients in the United States, subsequent treatment modifications, hospitalizations and the impact of hospitalizations on therapy changes, and treatment adherence and persistence.

METHODS: Using medical and pharmacy claims data from the Truven Health MarketScan database, this retrospective cohort study included adult patients with ≥ 2 medical claims corresponding to an HF diagnosis (ICD-9-CM codes 428.x, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, and 404.93) between April 2009 and March 2012. The date of the first claim was defined as the index date. Patients with continuous medical and pharmacy eligibility for a minimum of 12 months pre- and post-index were included in the analysis. Patients with an HF diagnosis in the 12 months before the index date were excluded. Index treatment (within 30 days post-index), subsequent treatment modification (class addition/removal) during the study period, hospitalization, and change in treatment after hospitalization (within 15 days after hospital discharge) were determined. Adherence was evaluated using the proportion of days covered (PDC) method, and persistence was defined as the proportion of patients remaining on index treatment after a defined period of time (12 months).

RESULTS: A total of 235,758 patients meeting the sample selection criteria were included in the analysis and were followed for a median of 28 months after the index date. Approximately 42% of patients were not prescribed any HF-specific treatment within 30 days post-index. Among those treated, prescriptions for ACEIs were filled by 46.42% of patients, ARBs by 17.07%, BBs by 75.62%, and AAs by 9.83%. Based on HF therapy class, monotherapy was prescribed to 51% of patients, bi-therapy to 40%, and triple therapy to 9%. More than 80% of patients experienced treatment modification during the median 28 months of follow-up. A total of 174,563 (74.0%) patients had at least 1 all-cause hospitalization (mean 1.11 [SD=0.98]) per year, with a mean length of stay (LOS) of 7.19 [SD=8.69] days. Within 12 months post-index, 85.7% of these patients experienced an all-cause hospitalization, with 29.6% having HF-related hospitalization (mean 0.18 [0.36]) and mean LOS of 5.85 [5.45] days. More than 60% of patients continued on the same therapy after all-cause or HF hospitalization. More patients on multiple therapies remained on the same treatment (73%-89%) compared with those treated with monotherapy (60%-73%) after the first HF hospitalization. Among patients untreated before hospitalization, 9.8% and 17% received treatment after all-cause and HF hospitalization, respectively. During the entire study

period (median 28 months), 29% of patients did not have a prescription fill for HF-specific treatments. The median PDC was >0.65 , and considering a gap of 30 days between ends of supply from 1 medication fill to the subsequent fill, persistence ranged from 41% (AA) to 52% (BB).

CONCLUSIONS: Findings of this claims database analysis among 235,758 HF patients suggest that more than one third of newly diagnosed HF patients do not receive HF-specific medication within 30 days following initial diagnosis. Despite ACCF/AHA recommendations of initiating treatment with a combination of 2 HF drug classes, only 40% of patients had a prescription fill for bi-therapy. Hospitalization did not have a major impact on HF therapy prescribing patterns. To our knowledge, this is the first study to establish the impact of hospitalization on HF-specific treatment among newly diagnosed patients. Adherence and persistence were moderate across all HF therapies of interest. This analysis reveals the need for further research to better understand the reasons for the demonstrated delay in HF treatment initiation and limited use of guideline-directed medical therapy after initial diagnosis.

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What is already known about this subject

- Heart failure (HF) is a global public health problem affecting an estimated of 5.7 million patients in the United States. Approximately 50% of patients who develop HF die within 5 years of diagnosis, and in the United States, more than 1 million hospitalizations annually are attributed to HF.
- American College of Cardiology Foundation/American Heart Association guidelines recommend a combination of angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor II blockers (ARB) and beta blockers (BB) for the management of HF. Aldosterone antagonists are recommended as an add-on therapy for all patients with persisting symptoms despite treatment with ACEIs/ARBs and BBs.
- Previous studies have shown that these therapies are often under prescribed.

What this study adds

- This large, population-based study reflects the real-world clinical practice and treatment adherence of over 200,000 HF patients in the United States.

What this study adds (*continued*)

- This study found that a substantial proportion of patients (42%) did not receive HF-specific medication within 30 days after diagnosis, and 29% of patients did not have a prescription fill for HF-specific treatments during the entire study period (median 28 months). This finding highlights the need for increased usage of guideline-directed medical therapy.
- Data on the impact of hospitalization on treatment showed that more than 60% of patients continued on the same therapy after all-cause or HF-related hospitalization. Among patients who were untreated before an all-cause hospitalization, 9.8% received treatment after the hospitalization, and 17% received treatment after an HF-related hospitalization.

In the United States, heart failure (HF) affects approximately 5.7 million adults, with 870,000 new cases per year.¹ The prevalence of HF is projected to approximately double by 2030.² HF is associated with increased morbidity and mortality and a high economic burden primarily driven by hospitalizations.^{3,4}

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines recommend a combination of angiotensin-converting enzyme inhibitors (ACEIs), or angiotensin receptor blockers (ARBs) if intolerant to ACEIs, and beta blockers (BBs) as first-line treatment for HF with reduced ejection fraction (HFrEF) patients. Since there is no evidence-based therapy for the treatment of HF patients with preserved ejection fraction (HFpEF), guidelines advise management of symptoms and comorbidities. Specific medications in these treatment classes are the cornerstone of HF treatment, since they have been proven to improve symptoms, increase survival, and decrease hospitalizations.³ In cases where patients require more management, aldosterone antagonists (AAs) are recommended in cases where patients are symptomatic despite treatment with ACEIs and BBs.

Unfortunately, although multiple studies have shown that there is an improvement in survival post-HF diagnosis, the 5-year mortality rate remains considerably high at 50%.^{1,5} HF is the first cause of hospitalization ahead of cancer and respiratory diseases in patients aged >65 years and accounts for 3% of all hospital admissions in the United States, with nearly 1 million hospitalizations annually.⁶⁻⁸ There is inconsistent evidence for trends in hospitalizations over time; recent AHA statistics report no change in prevalence of HF hospitalizations from 2000 to 2010.¹ However, past studies report a decline in primary HF hospitalizations during the periods from 1998 to 2007 and 2001 to 2009.^{9,10}

Despite published recommendations from the ACCF/AHA, various studies have shown that HF patients are suboptimally managed, and treatment guidelines are often not followed in

clinical practice.¹¹⁻¹⁴ Furthermore, multiple comorbidities add complexity to the effective disease management of HF patients. Cumulatively, these result in adherence and persistence challenges, which may have negative implications for HF care and treatment outcomes.

The objective of this study was to examine treatment initiation patterns and subsequent treatment modifications, hospitalizations and the impact of hospitalizations on therapy changes, and medication adherence and persistence among newly diagnosed HF patients in a U.S. real-world setting.

Methods

Study Design and Data

A retrospective observational study was conducted using administrative claims data from the Truven Health MarketScan Commercial Claims and Encounters (CCAE) database and the Medicare Supplemental and Coordination of Benefits database.

The CCAE database contains employer-sponsored private health insurance records encompassing employees and their spouses and dependents. The Medicare Supplemental and Coordination of Benefits database contains the data of retirees with employer-sponsored Medicare supplemental insurance.¹⁵ MarketScan databases are in compliance with the Health Information Portability and Accountability Act of 1996 (HIPAA). The MarketScan claims data used in the current analysis covered the period from April 1, 2008, to September 30, 2013, since this was the most recent data available at the time of this analysis.

Sample Selection

Adult patients (>18 years of age) with at least 2 medical claims within 12 months on different dates corresponding to a HF diagnosis during the period from April 1, 2009, to March 31, 2012, were identified. The date of the first of these claims was defined as the index date (Figure 1). HF diagnosis was based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 428.x, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, and 404.93. Patients were required to have continuous enrollment in the database for 1 year before the diagnosis of congestive HF and at least 1 year of follow-up data after the index date. To ensure that prevalent patients were not included, patients with HF diagnosis in the 12 months pre-index period were excluded. Patients with multiple comorbidities were not excluded.

Study Variables

Patient characteristics assessed at the index date included age, gender, region, health insurance plan type, and employment status. Patient history was identified using ICD-9-CM codes, and the Charlson Comorbidity Index (CCI) was calculated for the 12-month pre-index period (baseline).

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FIGURE 1 Study Design

CHF = congestive heart failure.

FIGURE 2 Schematic Presentation of Algorithm Applied in the Definition of Index Treatment Combination

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker.

Drug treatment at index and end of follow-up was identified for the following treatment classes: ACEI, ARB, AA, BB, and diuretics (any). Diuretics were not included in combination treatments, since they are not disease-modifying drugs and are given mainly for management of symptoms. Due to the unavailability of dosage information in the database, treatment modifications were assessed only at the class level. Patients were grouped based on the number of treatment classes prescribed: monotherapy (1 treatment class), bi-therapy (a combination of 2 treatment classes), triple therapy (a combination of 3 treatment classes), and quadruple therapy (a combination of 4 treatment classes). The criteria for qualifying index treatments were as follows (Figure 2):

- The earliest drug class used was set as index therapy.
- Index therapy included drugs taken for at least 14 days within 30 days of index date.
- Other drug classes started within 14 days of index therapy, and continued together with index therapy for at least 14

days, were added to the index therapy and considered as combination treatment.

Device treatment such as implantable cardioverter defibrillator (ICD)/cardiac resynchronization therapy (CRT) was also identified. First treatment modification (defined as a change in treatment class or a change of combination [a new treatment class added or removed]) and time from index until the first treatment modification were evaluated.

All-cause and primary HF-related hospitalizations were estimated after the index date, with index date inclusive, and treatment transition after hospitalization (within a 15-day period of hospital discharge) was determined. Hospital treatment changes were only assessed if the data were available before and after hospitalization.

Adherence was evaluated using the proportion of days covered (PDC) method.¹⁶ Persistence was defined as the proportion of patients remaining on index treatment after a defined period

FIGURE 3 Patient Selection Process

HF = heart failure.

of time (12 months). A treatment gap period of a maximum of 30 days was regarded as acceptable between the end of supply from 1 medication fill to the subsequent fill.¹⁶

Analysis

Data were summarized using descriptive analyses. For categorical variables, counts and percentages were provided for each treatment class.

Results

After inclusion and exclusion criteria were met, 235,758 newly diagnosed HF patients comprised the study cohort (Figure 3). Patients were followed up for a median of 28 months (range = 12.2–54.8 months) after the index date.

Baseline Characteristics

A summary of patient demographics and clinical characteristics is presented in Table 1. Mean age of the study cohort was 70.9 years (standard deviation [SD] = 14.1) with 46.5% of the patients aged ≥75 years. There was a relatively even gender split with male patients comprising 51.6% of the cohort. Similar percentages of patients were from the North Central region (31.3%) and South region (30.2%).

The majority of patients in the study cohort had a history of essential hypertension (69.9%), followed by type 2 diabetes

(37.3%) and atrial fibrillation (28.3%). An equal percentage of patients had a CCI of 1 and 4+ (24.7% and 24.8%, respectively).

Treatment Initiation Pattern

Overall, 41.8% (n = 98,630) of patients did not have any single prescription fill for HF-specific treatments of interest (ACEIs, ARBs, BBs, and AAs) within 30 days of their first diagnosis. Even after taking diuretics into consideration, there were 35.5% (n = 83,710) of patients who did not have a treatment prescribed within 30 days of initial diagnosis. Among patients treated with HF-specific treatments (n = 137,128), prescriptions for ACEIs were filled by 46.42%, ARBs by 17.07%, BBs by 75.62%, and AAs by 9.83%. Overall, 51.3% of patients had prescription fills for monotherapy, and 40% for bi-therapy (Figure 4). Among the treated cohort, BB prescription fills were the most common monotherapy fills (29.8%), followed by ACEI (13.6%), ARB (6.3%), ACEI/ARB (19.9%), and AA (1.6%) fills. Prescriptions for bi-therapy of ACEI + BB were filled by 28.2% of patients, ARB + BB by 9.4%, and BB + AA by 2.4%. Prescriptions for the triple therapy combination of ACEI + BB + AA were filled by 4.4% of patients and ARB + BB + AA by 1.2%. In total, 66.1% of the treated patients had at least 1 prescription fill for ACEIs/ARBs, 76.8% for BBs, and 11.1% for AAs during the first 30 days after diagnosis.

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TABLE 1 Demographic and Clinical Characteristics of Patients with HF at Index

Characteristic	N = 235,758	
Age, years, mean (SD)	70.9	(14.1)
18-64, n (%)	81,060	(34.4)
65-74, n (%)	45,038	(19.1)
75+, n (%)	109,660	(46.5)
Male, n (%)	121,693	(51.6)
Region, n (%)		
Northeast	43,618	(18.5)
North Central	73,894	(31.3)
South	71,115	(30.2)
West	41,669	(17.7)
Unknown	5,462	(2.3)
Plan type, n (%)		
PPO	93,577	(39.7)
Comprehensive	87,901	(37.3)
HMO	29,648	(12.6)
POS	11,377	(4.8)
CDHP	3,606	(1.5)
EPO	1,902	(0.8)
HDHP	519	(0.2)
POS with capitation	519	(0.2)
Missing/unknown	6,190	(2.6)
Employment status, n (%)		
Medicare eligible retiree	78,705	(33.4)
Active full time	24,109	(10.2)
Surviving spouse/dependent	14,262	(6.0)
Retiree (status unknown)	14,004	(5.9)
Early retiree	9,856	(4.2)
Other/unknown	93,348	(39.6)
Medical history, %		
Hypertension	69.9	
Type 2 diabetes	37.3	
Atrial fibrillation	28.3	
COPD	23.9	
Renal impairment/failure	22.9	
Stroke	20.1	
Myocardial infarction	13.3	
Charlson Comorbidity Index, n (%)		
0	39,335	(16.7)
1	58,229	(24.7)
2	46,027	(19.5)
3	33,773	(14.3)
4+	58,394	(24.8)

CDHP = consumer-driven health plan; COPD = chronic obstructive pulmonary disease; EPO = exclusive provider organization; HDHP = high-deductible health plan; HF = heart failure; HMO = health maintenance organization; PPO = preferred provider organization; POS = point of service; SD = standard deviation.

In addition to the specific HF treatment classes, 74.8% of patients had prescription fills for diuretics. Prescription fills for fixed dose combinations of ACEIs (3.0%) or ARBs (4.3%) were limited. Usage of ICD/CRT was also limited, with only 2% of patients having an ICD/CRT-related claim.

Treatment Modifications

Among patients treated at index, treatment modification (initiation, discontinuation, or modification of treatment) at the end of the post-index follow-up period (median 28 months) was reported in more than 80%. The median time to first treatment modification was 3.0 months (range = 2.1 months for AAs to 3.3 months for BBs) for patients receiving monotherapy; 3.6 months (range = 2.6 months for BB+AA to 3.8 months for ARB+BB) for bi-therapy; 3.2 months for triple therapy; and 1.4 months for patients receiving quadruple therapy of ACEI+ARB+BB+AA.

The most frequent treatment modifications observed at the end of the follow-up period are presented in Figure 5. De-escalation of therapy during follow-up was reported for the majority of patients, with those on bi-therapy and triple therapy transitioning to monotherapy and bi-therapy, respectively. The most common transitions for patients on monotherapy were as follows: ACEI to ACEI+BB (27.1%), ARB to ARB+BB (25.9%), AA to AA+BB (17.8%), and BB to BB+ACEI (17.5%). The cumulative proportion of patients with an ICD/CRT-related claim in the post-index period was 3.9% at 1 year, 4.7% at 2 years, 5.0% at 3 years, 5.2% at 4 years, and 5.2% at 5 years.

Among initially untreated patients (n=98,630), 31.4% of patients received treatment after a median of 4.7 months. Specifically, these patients received BB monotherapy (44.6%), ACEI monotherapy (21.8%), or ARB monotherapy (9.8%). Of the total study cohort, 29% of patients (n=67,672) did not have a prescription fill for HF-specific treatments (ACEI, ARB, BB, or AA) during the entire study period (median 28 months). After including diuretics, there were still 24.9% of patients (n=58,812) without a prescription fill during the entire study period.

Hospitalizations and Change in Treatment

A total of 174,563 (74.0%) patients had at least 1 all-cause hospitalization with a mean of 1.11 (SD=0.98) hospitalizations per year and length of stay (LOS) of 7.19 (8.69) days. Of these 174,563 patients, 149,593 (85.7%) patients were hospitalized within the first 12 months. Similarly, 51,635 (21.9%) patients had HF-related hospitalizations, with a mean of 0.18 (0.36) hospitalizations per year and mean LOS 5.85 (5.45) days.

Overall, 80.5% of patients continued on the same treatment regimen following the first all-cause hospitalization (within 15 days). Transitioning to ACEI+BB bi-therapy was reported in 13% and 6% patients initially treated with ACEI or BB monotherapy, respectively (Figure 6). Among patients on bi-therapy with BBs, transitioning to BB monotherapy was the most frequent treatment modification. Of the untreated patients, 9.8% received treatment after all-cause hospitalization.

Following the first HF-related hospitalization, no change in treatment was observed for 74.7% of the patients. More patients on bi- and triple therapy remained on the same

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FIGURE 4 Treatment Distribution Among Incident HF Patients at Index (Within 30 Days)

AA = aldosterone antagonist; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker; HF = heart failure.

FIGURE 5 Top 2 Treatment Modifications at End of Follow-up Period

Note: Horizontal bars represent the proportion of patients that underwent treatment modifications at the end of follow-up (the top 2).

AA = aldosterone antagonist; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker; HF = heart failure.

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FIGURE 6 Percentage of Patients Switching to Another Combination After First All-Cause Hospitalization (the 2 Most Frequent Changes)

Note: Horizontal bars represent the number of patients that switched treatments (the top 2) after first all-cause hospitalization.

AA = aldosterone antagonist; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker; HF = heart failure.

treatment (73%-89%) compared with those patients treated with monotherapy (60%-73%; Figure 7). Among patients on ACEI or BB monotherapy, 21% and 10% transitioned to ACEI+BB combination, respectively. Of patients on bi-therapy with BBs, the 2 most frequent transitions were switching to triple therapy, followed by switching to BB monotherapy. Among patients who were untreated before HF-related hospitalization, 17% received treatment after HF-related hospitalization.

Adherence and Persistence

Median PDC across HF treatment classes was above 0.65 (Table 2). For all 4 main treatment classes (ACEI, ARB, BB and AA), persistence ranged from 41% (AA) to 52% (BB). The findings did not change substantially when the gap period was increased to 45 days (range=46%-60%) or 60 days (range=49%-65%; Table 2).

Discussion

This real-world study presents findings on treatment initiation patterns, treatment modifications, the impact of hospitalization on treatment, and medication adherence for newly diagnosed HF patients based on administrative claims. The analysis highlights that a substantial proportion of newly diagnosed HF patients (41.8%) did not have a claim for guideline-recommended HF treatment (ACEI, ARB, BB or AA) within 30 days after diagnosis. Furthermore, 29% of patients did not receive HF therapy by the end of the post-index follow-up, thereby reinforcing findings from previous studies that HF treatments are likely underutilized in the real world.^{11,12} Treatment modification was frequent and was reported in more than 80% of the patients. The median time to first treatment modification ranged from 1.4 months to 3.8 months. In addition, hospitalization was not associated with a change in treatment within 15 days of discharge in >70% of patients.

FIGURE 7 Percentage of Patients Switching To Another Combination After First HF Hospitalization (the 2 Most Frequent Changes)

Note: Horizontal bars represent the number of patients that switched treatments (the top 2) after first HF-related hospitalization.

AA = aldosterone antagonist; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker; HF = heart failure.

As previously noted, 41.8% of the patients did not have a prescription fill for HF-specific treatment (ACEI, ARB, BB, or AA) within 30 days after diagnosis. This might be partly explained by the inability of the administrative claims database to distinguish New York Heart Association (NYHA) class or to differentiate between HFpEF versus HFrEF patients. Hence, the sample is inclusive of NYHA class I patients, as well as those with HFpEF, for whom there is no approved therapy. Of these untreated patients, 31.4% received treatment after a median of approximately 4 months, suggesting a delay in HF treatment initiation. Overall, 29% of patients in the study cohort remained untreated at the end of follow-up. An earlier retrospective analysis based on a longitudinal, patient-level database studied patients from January 1, 1997, to December 31, 1999. This study also reported that 32.3% of patients did not receive any of the HF therapies (ACEI, BB, loop diuretics, or digoxin).¹⁴

Despite guideline recommendations to initiate treatment with bi-therapy of ACEIs (ARBs in patients with intolerance to ACEIs) and BBs, more patients had a prescription fill for monotherapy (51.4%) than bi-therapy (40%). However, since the analysis included incident patients, the percentage of patients on bi-therapy seems acceptable. Given the age of patients at baseline (mean age 70.9 years), the increased prevalence of contraindications and comorbidities in elderly patients may explain the lower rate of ACEI/ARB vs. BB prescription fills. Other studies evaluating prescription dispensing patterns in a community setting or using administrative claims databases reported similar findings.¹⁷⁻¹⁹ The study using data from the National Ambulatory Medical Care Survey reported usage of ACEIs/ARBs by 32% of patients and BBs by 38%, which is lower than the values reported in our study.²⁰ Among the registry-based studies, the findings from the “Get With the Guidelines-Heart Failure (GWTG-HF) Registry” were

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TABLE 2 Adherence and Persistence to HF Medications

	ACEI	ARB	AA	BB
PDC, median (range)	0.759 (0.01-1.00)	0.825 (0.01-1.00)	0.654 (0.01-1.00)	0.886 (0.01-1.00)
Persistence rate, 30-day gap, %	44.7	47.4	41.0	52.2
Persistence rate, 45-day gap, %	50.5	53.7	45.8	59.8
Persistence rate, 60-day gap, %	54.3	57.7	49.0	64.8

AA = aldosterone antagonist; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor II blocker; BB = beta blocker; HF = heart failure; PDC = proportion of days covered.

consistent with our study,²¹ whereas data from the IMPROVE-HF registry were relatively higher.²² The differences seen in our study compared with the observational registries mentioned may reflect the clinical quality improvement objective present in the scope of most registries. Hence, the practice patterns observed in such registries may be reflective of a more intensively managed population. Our study includes data from privately insured individuals across a variety of practice settings, including nonteaching and nonurban outpatient clinics, whereby many factors including patient adherence, socioeconomic influences, and physician awareness of guidelines may impact treatment patterns.

The baseline usage of ICD/CRT was 2.0%, and there was no substantial increase during the study follow-up (5.2% at 5 years post-index). This ICD/CRT rate is lower compared with other studies. The study based on the GWTG-HF registry reported a usage of 19.4% for ICD and 14.8% for CRT.²¹ This difference can be explained by the fact that our study included a relatively healthier, newly diagnosed population.

Over the study period, treatment modifications were reported in more than 80% of patients, with the majority reporting de-escalation in therapy. This is an interesting finding, and although it can be argued that this is because of the inclusion of patients with mild HF symptoms, we cannot rule out the possibility of other potential reasons, such as lack of adherence by patients, treatment tolerability, frequent comorbidities, depression, and various economic and administrative reasons. It should be noted that since information on dosage was unavailable in the database, treatment modifications are assessed only at the class level.

In the United States, 3% of all hospital admissions have HF as a primary diagnosis.⁶ Hospitalization is the key cost driver and accounts for 60%-70% of the direct medical costs of HF treatment.² The main determinant of HF hospitalization cost is LOS, with a recent review reporting a median LOS less than 5 days for an acute HF episode in North America.²³ Furthermore, each additional day of initial hospital stay is associated with a significant risk of rehospitalization and mortality within 30 days and 1 year.²⁴ Therefore, treatments aiming at reducing HF-related hospitalization will help in limiting overall HF-related health care costs. Compared with LOS data from the OPTIMIZE-HF registry (mean = 5.7, SD = 5.9 days),²⁵ the

mean LOS of 7.19 (SD = 8.69) days for all-cause hospitalizations was higher in the data presented here. However, the mean LOS of 5.85 (SD = 5.45) days for HF-related hospitalizations was similar to those reported in the published literature (5.27 to 6.3 days).^{9,26}

In the current study, hospitalization did not appear to have a major impact on the prescribing pattern, with 80% and 74% of patients continuing on the same treatment after all-cause and HF-related hospitalizations, respectively. It should be noted that patients with index hospitalizations will have more changes in treatment, since these are newly diagnosed patients. Contrary to this, patients with post-index hospitalizations would be expected to have comparatively fewer changes in treatment. A previous study based on the GWTG-HF registry also reports that the majority of patients continued the guideline-recommended medical therapy from hospital admission to discharge.²¹ Of the patients with no HF therapy pre-hospitalization, only 9.8% and 16.9% started treatment after all-cause and HF-related hospitalizations, respectively. These rates may be explained by either the short time window of 15 days after hospitalization used to identify treatment initiation, or the physician might see the patient within 15 days; however, the fill date might be later than the 15-day window, or the physician might prescribe an increase/decrease in the dose of certain medications, which did not constitute a treatment modification (as per the study definition). Because of the nature of information in the database, details regarding the inpatient treatment could not be collected.

Medication adherence is a modifiable factor that may contribute to increased rates of hospitalization and readmission in HF patients.²⁷ The cut-off for an adherence rate associated with significant improvement in survival is 88% in HF patients.²⁸ Adherence estimates in the literature vary considerably, ranging from 40% to 94%; this variability is attributed to the method of adherence measurement and the population under consideration. The PDC in this study ranged from 0.65 to 0.87, suggesting that patients had moderate to good adherence. It should be noted that claims data reflect prescription fills for medications (regimens); therefore, the data presented would be impacted by patient nonadherence in filling and refilling their prescriptions.

Limitations

Several limitations should be acknowledged when interpreting the results from this study. ICD-9-CM codes were used to identify HF diagnosis—they might not mirror confirmed clinical diagnoses and lack details to evaluate severity of illness (NYHA classification was not reported in the database). Additionally, the study cohort could not be categorized by type of HF (e.g., acute, chronic, rEF, or pEF). Therefore, the lack of clinical data on HF type and NYHA class does not allow for proper interpretation of the results and may have under- or overestimated the findings. Development of an algorithm to predict the diagnosis of HF patients will be useful while conducting such database studies. Furthermore, it is not certain whether the first recorded HF diagnosis code is when HF was truly diagnosed. Changes in index treatment combination do not account for modification of doses. Duration of therapy might have been underestimated owing to dropouts from the database. For patients who experienced index hospitalization, data on treatment before hospitalization were not available; therefore, they were not considered for the calculations. As previously noted, claims data reflect fills for the medication; therefore, the data presented are an estimate of patient non-adherence to fill the medication. Patients were not categorized as medication eligible or noneligible because of lack of clinical data; therefore, the prescription fill pattern was not estimated according to eligibility. Hence, the presented data may appear different compared with other studies that assessed eligibility. Although the patient population is derived from nationally representative groups of patients, it may not be generalizable beyond the commercially and Medicare supplement insured patient groups.

Despite these limitations, our study has considerable strengths. First, the study shows the impact of hospitalization on HF-specific treatment among newly diagnosed HF patients. Second, this large, population-based study reflects the real-world clinical practice and treatment adherence of over 200,000 HF patients in the United States. Last, persistence to medication was assessed using multiple gap periods (30 days, 45 days, and 60 days), since there is no recognized standard to assess this parameter.

Conclusions

Findings of this representative claims database analysis among 235,758 HF patients suggest that more than one third of the patients do not receive HF-specific medication within 30 days following initial HF diagnosis. Despite ACCF/AHA recommendations to initiate treatment with a combination of 2 HF drug classes, only 40% of patients had a prescription fill for the same. Hospitalization did not appear to have a major impact on HF therapy-prescribing patterns. To our knowledge, this is the first study to evaluate the impact of hospitalization on HF-specific treatment among newly diagnosed patients.

Adherence and persistence were moderate across all HF therapies of interest. This analysis reveals the need for further research in order to better understand the reasons for the demonstrated delay in HF treatment initiation and limited use of guidelines-recommended combination therapies after initial diagnosis. Investigation of the effect of this delayed therapy initiation on patient outcomes is also warranted.

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DISCLOSURES

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Concept and study design were contributed by Deschaseaux, Hudson, and Turner, along with McSharry. McSharry took the lead in data collection, along with Deschaseaux, Hudson, and Turner. Data interpretation was performed by Hudson, along with the other authors. The manuscript was written by Agrawal, along with Deschaseaux and Turner, and revised by Deschaseaux and Turner, along with the other authors.

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