Hospitalizations After Heart Failure Diagnosis

A Community Perspective

Shannon M. Dunlay, MD,* Margaret M. Redfield, MD,* Susan A. Weston, MS,† Terry M. Therneau, Ph.D,† Kirsten Hall Long, Ph.D,† Nilay D. Shah, Ph.D,† Véronique L. Roger, MD, MPH*† Rochester, Minnesota

Objectives

The purpose of this study was to determine the lifetime burden and risk factors for hospitalization after heart failure (HF) diagnosis in the community.

Background

Hospitalizations in patients with HF represent a major public health problem; however, the cumulative burden of hospitalizations after HF diagnosis is unknown, and no consistent risk factors for hospitalization have been identified.

Methods

We validated a random sample of all incident HF cases in Olmsted County, Minnesota, from 1987 to 2006 and evaluated all hospitalizations after HF diagnosis through 2007. International Classification of Diseases-9th Revision codes were used to determine the primary reason for hospitalization. To account for repeated events, Andersen-Gill models were used to determine the predictors of hospitalization after HF diagnosis. Patients were censored at death or last follow-up.

Results

Among 1,077 HF patients (mean age 76.8 years, 582 [54.0%] female), 4,359 hospitalizations occurred over a mean follow-up of 4.7 years. Hospitalizations were common after HF diagnosis, with 895 (83.1%) patients hospitalized at least once, and 721 (66.9%), 577 (53.6%), and 459 (42.6%) hospitalized 2, 3, and 4 times, respectively. The reason for hospitalization was HF in 713 (16.5%) hospitalizations and other cardiovascular in 936 (21.6%), whereas over one-half (n = 2,679, 61.9%) were noncardiovascular. Male sex, diabetes mellitus, chronic obstructive pulmonary disease, anemia, and creatinine clearance <30 ml/min were independent predictors of hospitalization (p < 0.05 for each).

Conclusions

Multiple hospitalizations are common after HF diagnosis, though less than one-half are due to cardiovascular causes. Comorbid conditions are strongly associated with hospitalizations, and this information could be used to define effective interventions to prevent hospitalizations in HF patients. (J Am Coll Cardiol 2009;54:1695–702)

An estimated 5.3 million Americans are living with heart failure (HF), and its prevalence has risen (1). Although improvements in mortality after HF diagnosis have been noted (2,3), hospitalizations related to HF have increased from an estimated 400,000 discharges in 1979 to nearly 1.1 million in 2005 (1). With growing numbers of patients living with HF and increasing hospitalizations, HF costs are significant, with 2008 U.S. estimated costs of $34.8 billion (1). Thus, HF constitutes a major public health problem, a large component of which is related to hospitalizations. Yet, little is known about the natural history of hospitalizations after diagnosis of HF. Further, data on the cause of hospitalization after HF diagnosis are sparse. Finally, it has been recently underscored that no consistent predictors of hospitalization in patients with HF have emerged, which hinders the development of effective interventions (4).

Although important knowledge has been gained from patients enrolled in HF clinical trials and from databases comprised of patients hospitalized with HF, these studies cannot fully appraise the total burden of hospitalization in patients with HF. Indeed, patients enrolled in clinical trials differ from the community because they are younger, more frequently male, and have low ejection fraction (EF) (5). Further, large HF registries and databases focus only on patients who have

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already been hospitalized for de-compensated HF (6–8) who may not represent the community, as hospitalization for HF has been shown to be a poor prognostic sign (9,10), and these patients may be at higher risk for subsequent HF hospitalizations (11). Finally, the use of prevalent cases and analysis of only short-term rehospitalization prevents examination of the cumulative lifetime burden of hospitalizations in patients after initial HF diagnosis.

To address these gaps in knowledge, we undertook the present study of incident HF cases diagnosed from 1987 through 2006 in a stable community setting to examine the frequency and causes of all hospitalizations that occurred over the course of a lifetime after HF diagnosis and whether changes have occurred over time. Second, we determined the risk factors for hospitalization after HF diagnosis.

Methods

Study design and setting. This study was conducted in Olmsted County, Minnesota, which has an estimated 2006 population of 137,521, 90% of whom are Caucasian. Population-based research is possible because there are few health care providers; the largest is Mayo Clinic. Medical records from all sources of care for residents are extensively indexed and linked via the Rochester Epidemiology Project (12). Herein, all patient-level information was obtained via the medical and administrative records. Patients were excluded from analysis if they declined to provide Minnesota Research Authorization. Studies were approved by the Mayo Clinic and Olmsted Medical Center institutional review boards.

Patient identification. Olmsted County residents with a possible HF diagnosis were identified using International Classification of Diseases-9th Revision (ICD-9) code 428 (HF). Codes are assigned based on physician diagnoses during outpatient visits or at hospital discharge. From all patients with ICD-9 code 428, a subset was randomly selected to undergo case validation and data abstraction. The HF index date was defined as the first evidence of HF in the medical record. Patients diagnosed with HF prior to the study period were excluded. Cases were validated using methods previously described (2). Abstractors reviewed records to ensure the HF episode met Framingham criteria. When utilized previously, missing data were minimal, and Framingham criteria could be applied in 98% of cases. The interabstractor agreement was 100%, indicating that these methods are highly reproducible.

Patient-level data. Baseline characteristics were abstracted from the medical record. Physician’s diagnosis was used to define hyperlipidemia, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, and peripheral vascular disease. Smoking status was classified as “current” or “prior/never.” Hypertension was defined by physician diagnosis, systolic blood pressure >140 mm Hg, or diastolic blood pressure >90 mm Hg. Diabetes mellitus was defined by blood glucose levels based on year-specific National Diabetes Data Group criteria (glucose ≥140 mg/dl since May 1972, ≥120 mg/dl from December 1958 to April 1972, and ≥130 mg/dl before December 1958) or use of diabetic medications. Prior myocardial infarction was defined using validated criteria (13). Body mass index was calculated using weight and height at HF diagnosis. The Charlson Index, a comorbidity score, was calculated (14).

Hemoglobin, creatinine, and EF at HF diagnosis (within 1 year) were abstracted. Anemia was defined as hemoglobin <13 mg/dl in men or <12 mg/dl in women (15). Creatinine clearance was estimated using the Modification of Diet in Renal Disease equation (16).

Study outcomes. Data on all-cause hospitalizations occurring after HF diagnosis from 1987 through 2007 were obtained through the Olmsted County Healthcare Expenditure and Utilization Database, which contains information regarding Olmsted County hospitalizations since 1987. For patients hospitalized at initial HF diagnosis, only subsequent hospitalizations were analyzed. In-hospital transfers or between the Olmsted Medical Center and Mayo Clinic hospitals were considered a single hospitalization. Hospital admissions within 1 day of the previous discharge were reviewed to determine whether they represented separate hospitalizations.

The principal diagnosis for each hospitalization was assessed using the primary ICD-9 code. This code, assigned by trained personnel after discharge, reflects the main reason for admission. Subsequent ICD-9 codes were not examined, as there is discretion in their number and order. The primary reason for hospitalization was divided into 1 of 3 categories (17,18): HF (ICD-9 codes, see the Online Appendix), other cardiovascular (ICD-9 390 through 459 except those used to define HF), or noncardiovascular (all other ICD-9 codes). Noncardiovascular codes were further grouped by type of problem.

Mortality follow-up occurred via the medical record. In addition to deaths noted in clinical care, the Mayo Clinic registration office records obituaries and local death notices, and death data are obtained from the State of Minnesota Department of Vital and Health Statistics quarterly.

Statistical analysis. Baseline patient characteristics are presented as percentages or mean (SD). Differences in baseline characteristics by sex were tested using the chi-square test for categorical variables or a 2-sample t test for continuous variables. The rate of hospitalization was examined by year of HF diagnosis (1987 through 1991, 1992 through 1996, 1997 through 2001, and 2002 through 2006) or by sex and was determined using the total hospitalizations divided by the person-years at risk for hospitalization. Differences were tested using Poisson regression. Trends in the length of stay...
According to year and differences by sex were analyzed using generalized linear models; length of stay was log transformed in analysis. The reason for hospitalization was examined overall, by year of HF diagnosis, and by sex. Trends in the reason for hospitalization by year of HF diagnosis were examined using the Mantel-Haenszel chi-square test; differences by sex were tested using the chi-square test. Andersen-Gill models (19) were used to identify the independent predictors of hospitalization. This technique allows all hospitalizations to be analyzed, in contrast to Cox modeling used in most studies that only consider the first hospitalization. Patients were censored at death or last follow-up. Missing data was 2% per variable with the exception of EF (n = 281 missing). Multiple imputation was used to impute missing values. Five datasets were created and analyzed, with results combined using Rubin’s rules (20). Analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, North Carolina) and S-PLUS version 8 (TIBCO Software Inc., Palo Alto, California). A p value of <0.05 was used as the level of significance.

**Results**

**Study population.** A total of 1,091 patients with incident HF were identified from 1987 through 2006. Fourteen patients, hospitalized at initial HF diagnosis, died during that hospitalization and were excluded from analysis as they were ineligible for subsequent hospitalizations, resulting in a study population of 1,077. The baseline characteristics are shown in Table 1. Compared with patients with reduced EF (<50%), patients with preserved EF (≥50%) were slightly older (77.8 vs. 77.3 years for preserved vs. reduced EF, respectively; p < 0.001) and more likely female (58.6% vs. 36.8% for preserved vs. reduced EF, respectively; p < 0.001). The proportion of patients with a Charlson comorbidity index ≥3 increased over the study period (p < 0.001). 

**Hospitalizations after HF diagnosis.** A total of 4,359 hospitalizations occurred during a mean (SD) follow-up of 4.7 (3.9) years. At study end, 798 (74.1%) patients had died. Hospitalizations after HF diagnosis were common (Fig. 1) and ranged from 0 to 42 (median: 3) per person. A similar number of hospitalizations per individual from heart failure (HF) diagnosis until death or last follow-up are shown.
distribution was observed among those who died, where hospitalizations ranged from 0 to 42 (median: 4) per person, indicative of lifetime hospitalizations after HF diagnosis. A total of 895 (83.1%) patients were hospitalized at least once, and 721 (66.9%), 577 (53.6%), and 459 (42.6%) were hospitalized 2, 3, and 4 times, respectively. Both HF and non-HF hospitalizations increased in the months prior to death (Fig. 2).

The mean rate of hospitalization was 86.6 per 100 person-years (95% confidence interval [CI]: 84.0 to 89.2). Thus, for each year after HF diagnosis, patients were hospitalized 0.87 times on average, or nearly once per year. Men were hospitalized more frequently, with 92.0 hospitalizations per 100 person-years (95% CI: 88.2 to 95.9) compared with 81.8 hospitalizations per 100 person-years (95% CI: 78.4 to 85.3) for women (p = 0.001). The rate of hospitalization after HF did not change over time.

The median length of stay per hospitalization was 5 (25th, 75th percentile: 3, 7) days. The length of stay declined over the study period, with median values of 6, 5, and 4 days for hospitalizations from 1987 through 1991, 1992 through 1996, 1997 through 2001, and 2002 through 2007, respectively (p for trend <0.001). Length of stay was similar among men and women (median: 5 days vs. 5 days, p = 0.40).

**Primary reason for hospitalization.** ICD-9 codes were missing in 31 of 4,359 (<1%) hospitalizations, leaving 4,328 included in the reason for hospitalization analysis (Table 2). HF was the primary reason for hospitalization in 713 (16.5%) hospitalizations, whereas 936 (21.6%) were due to other cardiovascular causes. Most hospitalizations (n = 2,679, 61.9%) were due to noncardiovascular causes. The primary cause of hospitalization did not differ by sex (p = 0.106), but changed over time (p < 0.001), with a decrease in the proportion of hospitalizations due to HF noted. The most common reasons for other cardiovascular hospitalizations were ischemic heart disease (ICD-9 410 through 414: 299 of 936 hospitalizations, 31.9%) and arrhythmias (ICD-9 427: 249 of 936 hospitalizations, 26.6%).

Reasons that accounted for >1% of noncardiovascular hospitalizations are shown in Table 3. Respiratory tract infections, chronic lung disease, and other respiratory symptoms accounted for a large proportion of noncardiovascular hospitalizations (30.4%). Bone and joint diseases accounted for an additional 11.0%. Comorbidities frequent in HF patients, including kidney disease, psychiatric disease, and diabetes mellitus, were additional common reasons for hospitalization.

**HF hospitalizations.** Although only 713 (16.5%) hospitalizations were due to HF, these were clustered among a fraction of the cohort, with just 348 of 1,077 (32.3%) patients ever having an HF hospitalization after diagnosis (hospitalization at the time of incident HF diagnosis excluded). Overall, 39.8% of patients with EF <50% were hospitalized for HF at least once compared with 34.0% of patients with EF ≥50% (p = 0.069). Among the 348 with an HF hospitalization, the number of HF hospitalizations ranged from 1 to 21, and 205 (58.9%) had 1, 67 (19.3%) had 2, and 76 (21.8%) had 3 or more. The incident HF patients with 2 or more HF hospitalizations (n = 143) accounted for the majority of HF hospitalizations (508 of 713, 71.2%). They were younger than the rest of the cohort (mean age 74.0 years vs. 77.2 years, p < 0.001), had higher body mass

**Table 2 Primary Cause of Hospitalization According to Year of Diagnosis and Sex**

<table>
<thead>
<tr>
<th>Type of Hospitalization, n (%)</th>
<th>Total Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF</td>
<td>Other CV</td>
</tr>
<tr>
<td>Overall</td>
<td>713 (16.5)</td>
</tr>
<tr>
<td>Year of HF diagnosis</td>
<td></td>
</tr>
<tr>
<td>1987–1991</td>
<td>210 (19.4)</td>
</tr>
<tr>
<td>1992–1996</td>
<td>225 (16.8)</td>
</tr>
<tr>
<td>1997–2001</td>
<td>184 (15.7)</td>
</tr>
<tr>
<td>2002–2006</td>
<td>94 (12.8)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>359 (16.7)</td>
</tr>
<tr>
<td>Female</td>
<td>354 (16.3)</td>
</tr>
</tbody>
</table>

CV = cardiovascular; HF = heart failure.
index (mean 31.1 kg/m² vs. 29.1 kg/m², p = 0.004), more frequently had diabetes (29.4% vs. 19.8%, p = 0.009), and less frequently had COPD (16.8% vs. 24.5%, p = 0.04). Other baseline characteristics were similar.

The length of stay for HF hospitalizations was similar to non-HF hospitalizations (median 4 [25th, 75th percentile: 3, 7] vs. median 5 [25th, 75th percentile: 3, 8] days, respectively; p = 0.064), and decreased over time with median values of 7, 5, 4, and 4 days for hospitalizations from 1987 through 1991, 1992 through 1996, 1997 through 2001, and 2002 through 2007, respectively (p for trend <0.001).

Risk factors for hospitalization after HF diagnosis. The univariate predictors of hospitalization are shown in Figure 3. Age, hypertension, diabetes, COPD, peripheral vascular disease, cerebrovascular disease, anemia, and decreased renal function were each univariately associated with an increased risk of hospitalization. In multivariable analysis, male sex, diabetes, COPD, anemia, and a creatinine clearance <30 ml/min were independent predictors of hospitalization (Fig. 4). Ancillary analysis examining “time to first” hospitalization after HF diagnosis using standard Cox modeling yielded similar results. In contrast to all-cause hospitalization, the independent predictors of a first HF hospitalization after diagnosis included diabetes (hazard ratio [HR]: 1.56, 95% CI: 1.20 to 2.02) and creatinine clearance 30 to <60 ml/min (HR: 1.42, 95% CI: 1.13 to 1.78). COPD was associated with a nonsignificant increase in risk of HF hospitalization (HR: 1.29, 95% CI: 0.99 to 1.68).

Discussion
In this community HF cohort, patients were hospitalized frequently after incident HF diagnosis over the course of their lifetime. The majority of hospitalizations were due to noncardiovascular causes, the most common being respiratory etiologies. Although HF was the primary reason for only 16.5% of hospitalizations, these were experienced by a small number of patients who often had repeated HF admissions. The independent risk factors for all-cause hospitalization were male sex, COPD, diabetes, anemia, and renal dysfunction.

Community burden of hospitalizations among incident HF patients. The number of HF hospitalizations has increased dramatically over the past several decades (1,21,22). Data from the National Hospital Discharge Survey suggests that hospitalizations with any mention of HF have tripled from 1.3 million in 1979 to 3.9 million in 2004 (21), and HF hospitalizations have become a major public health burden. Community studies indicate that although the incidence of HF has remained stable over time, survival has improved, leading to an increase in the prevalence of HF in the U.S. (2,3), which suggests that the increase in HF hospitalizations reflects, in
part, the larger population of patients. Yet, little is known about the burden of hospitalization among HF patients, including the rate and cumulative number of hospitalizations per patient that occur after HF diagnosis and whether temporal changes have occurred. Studies have suggested that readmission rates are high in patients with a prior HF admission...
HF patients are elderly and have a high burden of comorbidities, which may necessitate hospitalization even if HF is well-treated, and second, addressing non-HF comorbidities may prevent hospitalizations in HF patients. **Risk factors for hospitalization after HF diagnosis.** Recent public health efforts have aimed to decrease hospitalizations in HF. Certainly, HF admission has emerged as a risk factor for hospital readmission (8). However, despite multiple studies, no consistent predictors of readmission among patients with HF have emerged (4). Though there are several studies evaluating models of readmission predictors after an HF admission (8,11,27,28), they have limited risk prediction to patients with a prior HF admission, have had short follow-up periods, and have restricted analyses to time-to-first hospitalization, thereby missing the cumulative burden of hospitalizations that may occur over the course of a lifetime after HF diagnosis. To the best of our knowledge, no studies have examined predictors of admission using incident-validated HF patients followed for a prolonged time period or used modeling techniques to account for repeated hospitalizations after HF diagnosis. As HF is a chronic disease characterized by periodic exacerbations often leading to multiple hospitalizations, analyzing only the first rehospitalization excludes information from subsequent hospitalizations. Herein, independent risk factors for all-cause admissions after HF diagnosis are male sex, diabetes mellitus, COPD, anemia, and reduced creatinine clearance at HF diagnosis. Detection of these factors among newly diagnosed HF patients may help in identifying those at highest risk for multiple admissions and for whom more intense care is needed. The fact that most hospitalizations among HF patients are due to non-HF causes underscores the urgent need to determine whether targeting comorbidities could lead to a decrease in hospitalizations. **Study limitations.** First, although all hospitalizations in the community were captured in our study, hospitalizations outside of the county were not included. However, as the county is relatively isolated, hospitalizations outside of the county are likely rare. Second, the use of ICD-9 codes to identify the cause of hospitalization may lead to some misclassification. However, ICD-9 codes for HF have not changed over the study period, and methods for determining primary ICD-9 codes to Mayo Clinic have remained constant and thus should not bias examination of secular trends. Whether the burden of hospitalizations observed in HF patients differs from the general elderly population was not examined, although patients admitted with HF have been demonstrated to have higher readmission rates than other diagnoses in the Medicare population (29). We cannot exclude that unmeasured characteristics such as medication adherence and clinical care, which were not evaluated, may impact hospitalizations. Further, an assumption of the Andersen-Gill model is that all hospitalizations have a common baseline hazard function. There is no clinical indication that this assumption does not hold. Lastly, although Olmsted County is becoming increasingly diverse, the population remains largely Caucasian, and hospi-

(8,23,24); however, these data may lack generalizability as they are limited to patients with an HF hospitalization, itself a poor prognostic sign (9,10).

The present study brings important new knowledge by examining hospitalizations over the course of a lifetime after incident HF diagnosis, thereby enabling us to report on the comprehensive experience of patients living with HF in the community. Our findings indicate that hospitalizations are common after HF diagnosis, occurring nearly once per year. The majority (83%) of HF patients experienced at least 1 hospitalization after diagnosis, and multiple hospitalizations were common. Further, the rate of admissions for individuals diagnosed with HF showed no signs of abatement in recent years. These findings are particularly striking, given the extensive efforts to reduce hospitalizations in HF (25), and raise the question of the cause of HF hospitalizations. **Primary reason for hospitalization.** Little is known about the etiology of hospitalizations among HF patients. Fang et al. (21) examined hospitalizations from the National Hospital Discharge Survey from 1979 through 2004. They found that the proportion of hospitalizations with HF as a first-listed diagnosis remained at approximately 30% over the study period. However, there was a decline in the proportion of admissions due to coronary or other cardiovascular diseases, and an increase in the proportion due to noncardiovascular diseases. Curtis et al. (8) examined hospital readmission rates among Medicare beneficiaries hospitalized with HF from 2001 through 2005 and found that approximately 27% of readmissions were due to HF. This analysis did not include patients without a prior HF hospitalization and only examined the first readmission, and thus cannot provide information on the total burden of hospitalizations. To date, the cause of hospitalization among community HF patients, and potential temporal changes, remain unclear.

The present analysis indicates that HF is the primary cause of hospitalization only 16.5% of the time. However, among patients with at least 1 HF hospitalization, repeat HF admissions are common, and a small proportion of HF patients account for the majority of HF admissions. Importantly, most hospitalizations were due to noncardiovascular causes (62%), and HF hospitalizations have decreased over time. There are several potential explanations for these findings. First, the prevalence of HF patients with preserved EF may have increased (26), and these patients often have more comorbidities that could lead to non-HF hospitalizations. Although patients with reduced EF experienced HF admissions more commonly than preserved-EF patients (40% vs. 34%, respectively), the difference was not significant. Second, the shift to non-HF causes of hospitalizations may be attributable to the observed increase in the burden of comorbidities among HF patients over time. Further, changes in diagnosis or coding patterns resulting in a shift from HF to other causes could not be excluded. The implications of these findings are 2-fold: first, community HF patients are elderly and have a high burden of comorbidities, which may necessitate hospitalization even if HF is well-treated, and second, addressing non-HF comorbidities may prevent hospitalizations in HF patients.
talizations after HF diagnosis may differ in other racial and ethnic groups. However, our study has several important strengths, including the use of a validated, incident, community HF population followed for a prolonged period of time, with the ability to capture all subsequent hospitalizations, thereby allowing us to assess the burden and risk factors for hospitalization after HF diagnosis.

Conclusions

As the costs of medical care in the U.S. continue to rise, decreasing hospitalizations among patients with HF is critically important. Our findings indicate that hospitalizations are common, occurring nearly once per year after diagnosis. However, the majority are due to noncardiovascular causes, with HF hospitalizations experienced by only one-third of all HF patients. The relationship between comorbidities and increased hospitalization risk, coupled with a shift toward non-HF–related causes, indicate that comorbidities play a central and increasing role in hospitalizations in patients with HF. These data have important implications for preventive efforts to reduce the burden of hospitalization among patients with HF. Indeed, to be effective, strategies aiming to reduce hospitalization must include the identification and management of comorbid conditions in addition to addressing HF manifestations.

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Reprint requests and correspondence: Dr. Véronique L. Roger, Department of Health Sciences Research, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905. E-mail: roger.veronique@mayo.edu.

REFERENCES


Key Words: heart failure • epidemiology • hospitalization • community • risk factors.

APPENDIX

For a table on the heart failure ICD-9 codes, please see the online version of this article.