CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Characteristics of Hospitalizations for Heart Failure with Preserved Ejection Fraction

Parag Goyal, MD,[a] Zaid I. Almarzooq, MD,[b] Evelyn M. Horn, MD,[a] Maria G. Karas, MD,[a] Irina Sobol, MD,[a] Rajesh V. Swaminathan, MD,[a] Dmitriy N. Feldman, MD,[a] Robert M. Minutello, MD,[a] Harsimran S. Singh, MD,[a] Geoffrey W. Bergman, MD,[a] S. Chiu Wong, MD,[a] Luke K. Kim, MD[a]

[a]*Division of Cardiology and* [b]*Department of Medicine, Weill Cornell Medical College, New York, NY.*

ABSTRACT

BACKGROUND: Hospitalizations for heart failure with preserved ejection fraction (HFpEF) are increasing. There are limited data examining national trends in patients hospitalized with HFpEF.

METHODS: Using the Nationwide Inpatient Sample, we examined 5,046,879 hospitalizations with a diagnosis of acute heart failure in 2003-2012, stratifying hospitalizations by HFpEF and heart failure with reduced ejection fraction (HFrEF). Patient and hospital characteristics, in-hospital mortality, and length of stay were examined.

RESULTS: Compared with HFrEF, those with HFpEF were older, more commonly female, and more likely to have hypertension, atrial fibrillation, chronic lung disease, chronic renal failure, and anemia. Over time, HFpEF comprised increasing proportions of men and patients aged ≥75 years. In-hospital mortality rate for HFpEF decreased by 13%, largely due to improved survival in those aged ≥65 years. Multivariable regression analyses showed that pulmonary circulation disorders, liver disease, and chronic renal failure were independent predictors of in-hospital mortality, whereas treatable diseases including hypertension, coronary artery disease, and diabetes were inversely associated.

CONCLUSIONS: This study represents the largest cohort of patients hospitalized with HFpEF to date, yielding the following observations: number of hospitalizations for HFpEF was comparable with that of HFrEF; patients with HFpEF were most often women and elderly, with a high burden of comorbidities; outcomes appeared improved among a subset of patients; pulmonary hypertension, liver disease, and chronic renal failure were strongly associated with poor outcomes.

 • *The American Journal of Medicine (2016) 129, 635.e15-635.e26*

KEYWORDS: Epidemiology; Heart failure; Mortality

Heart failure is typically dichotomized into the traditional disease state caused by a reduced ejection fraction, and heart failure with preserved ejection fraction (HFpEF), where cardiac dysfunction in the absence of a depressed ejection fraction can also cause dyspnea, fatigue, and volume overload. In the current era, the number of patients hospitalized with HFpEF is comparable with that of heart failure with reduced ejection fraction (HFrEF) and is expected to exceed that of HFrEF in the next few years.[1] Despite increased attention and recognition over the past 2 decades, HFpEF has been particularly challenging to describe, given its diverse etiologies and presentations. Even definitions and terminology have been an area of debate.

As a result, while the literature is replete with studies dedicated to characterizing HFrEF, far less is known about HFpEF. Whereas registries[2,3] and community-based studies[4-9] have provided some insight on characteristics and outcomes of hospitalized patients with HFpEF, reports have been subject to selection bias or have been confined to particular regions of the country, limiting their generalizability. There is

Funding: This work was supported by grants from the Michael Wolk Heart Foundation and the New York Cardiac Center, Inc. The Michael Wolk Heart Foundation and the New York Cardiac Center, Inc had no role in the design and conduct of the study.

Conflict of Interest: DNF has received consulting/speaker's fees from Eli Lilly, Daiichi-Sankyo, Abbott Vascular, Pfizer, and Bristol-Myers Squibb. The other authors report no conflicts.

Authorship: All authors had access to the data and a role in writing the manuscript.

Requests for reprints should be addressed to Parag Goyal, MD, Division of Cardiology, Department of Medicine, Weill Cornell Medical College, 520 East 70th Street, New York, NY 10021.

E-mail address: pag9051@nyp.org

0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2016.02.007

a need for studies that analyze HFpEF on a national scale, capable of reporting on the population's inherent heterogeneity[10] using a broadly inclusive cohort, as such studies offer the promise of filling the gaps of knowledge that remain in the understanding of HFpEF, a disease process that still lacks proven therapies. Examining the Nationwide Inpatient Sample,[11] we aimed to characterize patients hospitalized with HFpEF in the US in 2003-2012. By analyzing each individual year of the study period, we also aimed to identify important temporal trends.

CLINICAL SIGNIFICANCE

- The number of hospitalizations for heart failure with preserved ejection fraction (HFpEF) was comparable with that of heart failure with reduced ejection fraction.
- Patients with HFpEF were most often women and elderly, with a high burden of comorbidities.
- Over time, in-hospital mortality rates and length of stay for HFpEF improved in a subset of patients.
- Pulmonary hypertension was the strongest correlate for in-hospital mortality.
- Treatable comorbidities were the strongest correlates for in-hospital survival.

METHODS

Data Source and Study Population

Data were obtained from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project—Nationwide Inpatient Sample files from 2003-2012.[11] The Nationwide Inpatient Sample is a 20% stratified sample of all nonfederal US hospitals. Hospitalizations were weighted based on a sampling scheme to permit inferences for a nationally representative population.[11] Each record in the Nationwide Inpatient Sample represented a patient hospitalization, and included all procedure and diagnosis International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes recorded for each discharge.

All hospitalizations with a diagnosis of acute heart failure among adults aged ≥18 years in 2003-2012 were included for analysis. Hospitalizations for HFpEF were identified based on presence of acute diastolic heart failure, ICD-9-CM codes 428.31 and 428.33. Hospitalizations for HFrEF were identified based on presence of acute systolic heart failure, ICD-9-CM codes 428.21 and 428.23.

Variable ejection fraction cutoffs differentiating HFpEF from HFrEF in clinical trials have created uncertainty about the mid-range or borderline ejection fraction, which some suggest represents a separate phenotype.[12] To avoid systematic bias of including this phenotype, those with combined acute systolic and diastolic heart failure were excluded from analysis.

Patient-level variables were obtained from the Nationwide Inpatient Sample database. The Agency for Healthcare Research and Quality comorbidity measures, based on the previously validated Elixhauser methods,[13] were used to identify comorbid conditions. Hospital characteristics were derived from the American Hospital Association Annual Survey Database. Outcome measures were obtained from the Nationwide Inpatient Sample database, and included in-hospital all-cause mortality and length of stay.

Statistical Analysis

Admission rates were calculated as the weighted number of hospitalizations for acute heart failure divided by 20% of the total number of US adults during the same periods. Estimates of the US adult population between 2003 and 2012 were obtained from the US Census Bureau.[14]

To compare baseline characteristics, Mann-Whitney Wilcoxon nonparametric tests or Student's *t* tests were used for continuous variables, and Pearson chi-squared tests were used for categorical variables. Pearson chi-squared tests were used to compare in-hospital mortality, and Student's *t* tests were used to compare length of stay. Temporal trends of baseline characteristics and outcomes were assessed using the autoregressive integrated moving average model for time series. Specified subgroups for analysis were determined a priori and were based on age, gender, race, race−gender, age−gender, and payer status.

Unadjusted rates of in-hospital mortality were calculated. Multivariable regression analyses were used to identify correlates of in-hospital mortality for HFpEF, and included patient-level variables (age, gender, race, payer status), hospital-level variables (size, geographic region, urban setting, academic status), and Elixhauser-based comorbidities including anemia, chronic lung disease, diabetes mellitus, hypertension, hypothyroidism, liver disease, neurodegenerative disorders, obesity, peripheral vascular disorders, pulmonary circulation disorders, collagen vascular disease, chronic renal failure, atrial fibrillation/flutter, coronary artery disease, valvular disease, prior coronary artery bypass grafting, and prior percutaneous coronary intervention. The Taylor linearization method "with replacement" design was used to compute variances for all regression analyses. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the fit of the logistic regression model. All statistical tests were 2-sided, and a *P*-value of $< .001$ was set to be statistically significant. All statistical analyses were conducted using SAS, version 9.2 (SAS Institute, Cary, NC) or SPSS, version 20 (IBM Corporation, Armonk, NY).

RESULTS

Population

Among 388,442,396 discharge records reviewed from 2003-2012, there were 5,046,879 hospitalizations with acute heart failure that met inclusion criteria. Patients were commonly female (52%), elderly (54% aged ≥75 years),