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STATE-OF-THE-ART PAPER

The Global Health and Economic Burden of Hospitalizations for Heart Failure

Lessons Learned From Hospitalized Heart Failure Registries

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Heart failure is a global pandemic affecting an estimated 26 million people worldwide and resulting in more than 1 million hospitalizations annually in both the United States and Europe. Although the outcomes for ambulatory HF patients with a reduced ejection fraction (EF) have improved with the discovery of multiple evidence-based drug and device therapies, hospitalized heart failure (HHF) patients continue to experience unacceptably high post-discharge mortality and readmission rates that have not changed in the last 2 decades. In addition, the proportion of HHF patients classified as having a preserved EF continues to grow and may overtake HF with a reduced EF in the near future. However, the prognosis for HF with a preserved EF is similar and there are currently no available disease-modifying therapies. HHF registries have significantly improved our understanding of this clinical entity and remain an important source of data shaping both public policy and research efforts. The authors review global HHF registries to describe the patient characteristics, management, outcomes and their predictors, quality improvement initiatives, regional differences, and limitations of the available data. Moreover, based on the lessons learned, they also propose a roadmap for the design and conduct of future HHF registries. (J Am Coll Cardiol 2014;63:1123–33)

Heart failure (HF) is a global public health problem affecting an estimated 26 million worldwide. In the United States alone, the prevalence is 5.7 million, and there are 670,000 new cases/year (1–3). Among the countries represented by the European Society of Cardiology (ESC), there are an additional 15 million patients with HF (4,5). Hospitalized heart failure (HHF) is the leading cause of hospitalization in the United States and Europe, resulting in over 1 million admissions as a primary diagnosis and representing 1% to 2% of all hospitalizations (2,6–8). Although the *per capita* HHF rate may be beginning to decline in the United States (6,9,10) and several European nations (11–13), the early post-discharge mortality and readmission rates have remained largely unchanged and may even be worsening.

Despite pre-defined inclusion/exclusion criteria, there are major regional differences in the severity, etiology, management, and outcomes of HHF patients in international clinical trials (14). However, hospital-based registries (15–26) remain

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Abbreviations and Acronyms

CCU = coronary care unit
ECG = electrocardiogram
EF = ejection fraction
HF = heart failure
HFpEF = heart failure with preserved ejection fraction
HFrEF = heart failure with reduced ejection fraction
HHF = hospitalized heart failure
ICU = intensive care unit
LOS = length of stay
NP = natriuretic peptide

the primary source of real-world data on HHF. Moreover, the data collected serve to identify unmet clinical needs in order to shape public policy at all levels and guide basic, translational, and clinical research endeavors. This review will provide an overview of global HHF registries including clinical characteristics, regional variation, and limitations of the available data. We also propose a conceptual framework for the design and conduct of future HHF registries to further our understanding of HHF and inform research efforts (27,28).

Patient Demographics and Clinical Characteristics

The mean age of patients admitted with a primary diagnosis of HF ranges from 70 to 75 years, with an SD of 15 years (Table 1). Regional variation in age is likely explained by differences in the prevalence of underlying risk factors as well as the standard of living. For example, patients participating in the major North American registries tended to be older than patients enrolled in countries with developing economies. In fact, the ADHERE-AP (Acute Decompensated Heart Failure National Registry International–Asia Pacific) registry found substantial variation in age of presentation among the 8 participating countries, which showed a strong inverse correlation with the human development index, a composite measure including life expectancy, adult literacy, educational level, and standard of living (25).

Approximately 40% to 50% of HHF patients are female, a group of patients that have traditionally been underrepresented in clinical trials (29), with 1 notable exception (30). The available data suggest that a larger proportion of HHF patients in the United States are female compared with other regions of the world. This is a noteworthy observation, as female patients are unique in that they tend to be older at the time of initial diagnosis and are more likely to have heart failure with preserved ejection fraction (HFpEF) (31). However, after adjusting for differences in baseline characteristics, women have comparable outcomes to men (32). There are virtually no data on race and ethnicity outside of the United States, and when collected, these data have traditionally been limited by the accuracy and completeness of provider documentation. Despite these shortcomings, African Americans and Hispanics make up approximately 20% and 7% of HHF patients, respectively, and tend to present at a younger age and have a lower ejection fraction (EF) and higher prevalence of medical comorbidities. Although the relative burden and severity of HF is greater in these vulnerable groups, HF care and risk-adjusted outcomes appear to be equitable in the context of multiple national hospital-based registries (33–35).

An ischemic etiology is universally the most common cause of HF, whereas HF secondary to uncontrolled hypertension, valvular pathology, and congenital heart disease are likely to be more common in the developing world. Depending on how the EF is categorized (i.e., 40% to 45%) and the population under consideration, 50% to 60% of the HHF population is classified as heart failure with reduced ejection fraction (HFrEF) (36). However, hospital-based registries conducted to date have not routinely measured EF during index admission. Thus, the true epidemiologic breakdown of HF patients by EF is unknown. More importantly, it is unclear what proportion of HFpEF patients previously had a reduced EF that improved in response to evidence-based therapies. In contrast to HFrEF, HFpEF is poorly characterized as a clinical entity, and there are currently no available evidence-based therapies, although medical comorbidities should be treated accordingly (36–38). Interestingly, there are some data based on the American Heart Association's GWTG-HF (Get With The Guidelines–Heart Failure) registry to suggest that the proportion of HHF patients classified as HFpEF is growing and may exceed HFrEF in the future (Fig. 1) (17). This may be due to increasing recognition of HFpEF by providers as well as demographic trends including aging of the population.

Importantly, cardiac and noncardiac comorbidities are extremely prevalent among HHF patients globally. More than one-half of all HHF patients have known CAD, which is complicated by myocardial infarction in 20% to 30% of cases, frequently resulting in systolic dysfunction. In addition, approximately 70% and 40% of HHF patients, respectively, have a history of hypertension and atrial fibrillation, and the prevalence of these comorbidities is even higher in HFpEF where they directly contribute to diastolic dysfunction and impaired ventricular filling. Similarly, noncardiac comorbidities including diabetes mellitus, chronic kidney disease, and chronic obstructive pulmonary disease may be found in over one-third of HHF patients. These conditions not only impact the pathophysiologic progression of HF but also limit the initiation and titration of evidence-based drug and diuretic therapy.

Although regional differences in comorbid conditions likely exist, the variation is less pronounced than would be expected based on clinical trial experience (14). However, because many of these comorbidities may represent either the inclusion or the exclusion criteria for enrollment in clinical trials, it is possible that they are most accurately characterized in a trial setting. Furthermore, medical comorbidities in hospital-based studies are generally self-reported, extracted from chart review and/or billing codes, and lack formal diagnostic criteria and objective evidence of the severity. In addition, other important comorbidities among HHF patients may be systematically underappreciated due to the lack of comprehensive screening and documentation efforts in clinical practice (e.g., sleep disorders and depression). Finally, therapies that may concurrently impact the management of HF (i.e., bronchodilators in chronic obstructive