

Outcomes in Patients with Heart Failure with Preserved Ejection Fraction

Katrina K. Poppe, PhD^a, Robert N. Doughty, MD, FRCP, FRACP, FCSANZ^{a,b,}*

KEYWORDS

• Heart failure • Reduced ejection fraction • Preserved ejection fraction

KEY POINTS

- Patients with HF-PEF represent between 30% and 50% of all patients with HF and are a heterogenous group of patients.
- Patients with HF-PEF have better survival but similar rates of hospital admissions as those with HF-REF.
- No current therapeutic interventions seem to improve the clinical outcomes for these patients and clinical management remains focused on relief of symptoms and management of comorbidities.

INTRODUCTION

Heart failure (HF) is a significant and increasing global public health problem. In the United States, it is estimated that currently 5.1 million adult Americans have HF, with projections that this will increase to more than 8 million by 2030.¹ The diagnosis of HF continues to be associated with poor quality of life, high morbidity, and high mortality despite contemporary HF management.^{2,3} Although survival for patients with HF has improved, mortality remains high, with approximately 50% dying within 5 years.^{1,4} Once admitted to hospital, patients experience high rates of subsequent HF hospitalization and mortality.²

HF is a clinical syndrome defined "clinically, as a syndrome in which patients have typical symptoms (eg, breathlessness, ankle swelling, and fatigue) and signs (eg, elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function."⁵ This clinically based

definition remains the encompassing definition of HF and is useful in clinical practice to identify the broad range of patients that can present with this syndrome. Importantly, indices of left ventricular (LV) systolic function, particularly LV ejection fraction (EF), are not used as criteria for this initial clinical diagnosis. The subset of HF patients with reduced EF (commonly termed HF-REF) has been extensively characterized; the pathophysiological mechanisms contributing to the progression of disease are now well understood, and therapeutic interventions, including pharmacobased and device-based therapies, are now well established in current HF clinical practice guidelines.⁵ The mortality for patients who receive all the available evidence-based therapies have been markedly reduced, with annual mortality in the large-scale clinical trials now being less than 6%.⁶ Numerous new therapeutic interventions are actively being studied for patients with HF-REF, which will further refine the management of this group of patients.

E-mail address: r.doughty@auckland.ac.nz

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^a Department of Medicine, National Institute for Health Innovation, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand; ^b Greenlane Cardiovascular Service, Auckland City Hospital, Private Bag 92024, Auckland 1142, New Zealand

^{*} Corresponding author. Department of Medicine, Level 12, Auckland Hospital Support Building, Park Road, Auckland, New Zealand.

Role of EF in HF

LV EF has an important role in HF management because EF is an important predictor of outcome and easily identifies the group of patients with systolic impairment (ie, HF-REF), and as such, guides the delivery of evidence-based therapies.⁵ However, many patients with HF have either normal or only mildly impaired EF, a group usually termed as heart failure with preserved ejection fraction or HF-PEF. The basic clinical characteristics of this group are now described: being more common among older women, with a history of hypertension, and less commonly, with a history of coronary artery disease. However, this group of patients has phenotypic heterogeneity, appears to have multiple underlying pathophysiological mechanisms, and frequently has multisystem disease.⁷ Importantly, patients with HF-PEF do not appear to gain the same benefits from neurohormonal antagonists as do those with HF-REF.8-10 As a result, further attention is being turned to the group of patients with HF-PEF.

Proportion of Patients with HF Who Have HF-PEF

Recent data from the United States have demonstrated that HF-PEF (defined here as EF \geq 50%) represented 36% of all patients with HF admitted to the "Get with the Guidelines" hospitals in the United States between 2005 and 2010.¹¹ A further 14% of patients had a borderline EF between 40% and 49%. Thus, patients with HF with EF greater than or equal to 40% represented half of all patients admitted during that time. A Canadian study of patients with HF reported similar proportions of patients based on EF criteria, with 31% having EF greater than or equal to 50%, and a further 13% having EF 40% to 49%.¹²

The proportion of HF patients who have HF-PEF appears to be increasing over time. For example, among patients hospitalized for HF between 1986 and 2002 in Olmsted County, MN, USA, the proportion of patients with HF-PEF increased from 38% to 54%.¹³ This increase was due to an increase in the absolute number of patients with HF-PEF (with the number of patients with HF-REF remaining relatively constant over that time period). Similarly, the proportion of HF patients with HF-PEF from 275 hospitals in the United States increased from 33% to 39% between 2005 and 2010.¹¹ It is thus clear from these and other data that HF-PEF is common, affecting between one-third to one-half of all patients with HF (depending on the cutoff of EF used to define this group of patients), and importantly, is increasing in prevalence.

CLINICAL OUTCOMES

HF has been known to be associated with high mortality and frequent hospital readmissions. During the 1980s and 1990s, hospitalizations for patients with HF initially increased in many countries and then decreased, and survival improved.^{3,14,15} Data from the United States also show that survival after a diagnosis of HF has improved over time, but overall mortality remains high with approximately 50% of patients dying within 5 years.⁴ One in 9 deaths in the United States has HF listed on the death certificate.¹ With the high morbidity and mortality for patients with HF, it is clinically important to understand these clinical outcomes among patients with HF-REF and HF-PEF.

In-Hospital Mortality

HF remains a common cause of hospitalization, with approximately 1 million admissions each year in the United States.¹⁶ Hospitalization with acute decompensated HF is a high-risk time for patients with HF with the potential for serious clinical events during that in-patient stay, including death. Two large-scale registries have reported inhospital outcome data for patients with HF-PEF compared with those with HF-REF. Data from the Acute Decompensated Heart Failure National Registry have shown that 50% of those patients admitted to hospital with acute HF had HF-PEF, although it was also notable that EF data were not available for approximately half of all the patients in this registry.¹⁷ The in-hospital mortality was lower for patients with HF-PEF compared with those patients with HF-REF (2.8% and 3.9%, respectively, P<.0001). The OPTIMIZE-HF Registry (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) reported data from 48,612 patients from 259 hospital in the United States, of whom 41,267 (84.9%) had EF data available.¹⁸ HF-PEF (here defined as EF \geq 40%) accounted for 51.2% of all patients with HF. The in-hospital mortality was lower for patients with HF-PEF compared with those patients with HF-REF (2.9% and 3.9%, respectively, P<.0001). Notably, the in-hospital mortality was similar for those with EF >50% and those with EF 40% to 50% (2.9% and 3.0%, respectively, P<.647).¹⁸ In summary, in-hospital mortality for patients with HF-PEF appears to be lower than for patients with HF-REF.

Long-Term Mortality

Over recent years, there has been uncertainty whether patients with HF-PEF have the same

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