Contemporary Approaches to Patients with Heart Failure

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KEYWORDS

• Heart failure with reduced ejection fraction • Heart failure with preserved ejection fraction
• Mortality • Guideline directed medical therapy

KEY POINTS

- Cohort and Medicare data reveal that incident heart failure and hospitalization for heart failure are decreasing. Furthermore, mortality among heart failure patients is increasingly due to noncardiovascular causes.
- Current evidence-based therapy for heart failure has improved heart failure–related mortality. Current efforts should be directed toward optimizing evidence-based medical and device therapy, reducing morbidity, and increasing the number of quality life-years with heart failure.
- In addition to the use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, implantable cardiac defibrillators, and cardiac resynchronization therapy to reduce mortality for heart failure with reduced ejection fraction (HFrEF), newer evidence supports the use of angiotensin receptor–neprilysin inhibitors and sinoatrial modulators to manage chronic stage C HFrEF.
- Innovations in regenerative therapy for HFrEF remain to be seen, whereas durable mechanical support is an established standard of care for end-stage heart failure as either destination therapy or a bridge to heart transplantation.
- Heart failure with preserved ejection fraction (HFpEF) remains without a specific indicated intervention that improves the natural history. The prevailing recommendation remains a focus on the associated comorbidities, for example, hypertension, atrial fibrillation, chronic renal disease, and obesity for which evidence-based interventions have been established. Future clinical trials should focus on therapies to reduce HFpEF mortality, especially as the burden of HFpEF is expected to exceed HFrEF in the coming years.

INTRODUCTION

It is estimated that 5.7 million adults are currently living with heart failure in the United States. That number is expected to exceed 8 million by 2030 with 915,000 new cases being diagnosed annually. Annual costs for heart failure care are expected to grow from $30.7 billion to $69.7 billion by 2030 as well.[1] Moreover, 1 in 5 adults are expected to develop heart failure after the age of 40, a rate that remains constant even among adults over the age of 80 in the remaining years of their lives. It is critical then to optimize care for heart failure given the increasing prevalence and cost of heart failure.

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Although 5-year mortality after a diagnosis of heart failure exceeds 50%, noncardiovascular causes account for more than 54% of deaths in heart failure patients.[1] Further prognostication and appropriate management of any heart failure patient require an understanding that heart failure is a syndrome and not a finite illness.

Dichotomizing heart failure patients as having HFrEF, defined as heart failure and a left ventricular ejection fraction $\leq$40%, or HFpEF, defined as heart failure with left ventricular ejection fraction $\geq$50%, has vital implications for subsequent care.[2] The current understanding of heart failure syndromes is evolving, with recent data identifying a separate new entity, *heart failure with recovered ejection fraction*, with at least separate prognostic implications from HFrEF and HFpEF.[3,4]

Temporal analyses from Olmstead County in Minneapolis reveal that between 2000 and 2010, incident heart failure rates *decreased* by 4.6% annually, with a greater reduction in incident heart failure of 45% for HFrEF and 28% for HFpEF.[5] Furthermore, hospitalizations and death for individuals with heart failure were driven primarily by noncardiovascular causes with slight improvements in all-cause 30-day readmission rates among Medicare beneficiaries.[5,6] A closer look at Medicare data reveals that, nationwide, hospitalizations for heart failure are declining by 3.1% annually with an overall reduction in the rate of hospitalization for heart failure by 30.5% between 1999 and 2011.[7] In aggregate, these trends reveal an emerging shift in emphasis to heart failure with preserved ejection fraction and the growing problem of recurrent hospitalization. Mortality however is improving as evidenced by years lived with heart failure.[5]

These measured successes may be attributed to the evidence-based, contemporary approaches to the management of heart failure syndromes formalized in the 2013 joint guidelines from the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) and in the more recently updated heart failure guidelines in the 2016 Focused Update.[2,8] Treatment of heart failure within these guidelines is recommended based on stages of heart failure, reflecting the development and progression of disease. Stage A heart failure refers to those individuals at high risk for heart failure yet exhibit no structural heart disease or symptoms of heart failure.[9] Stage B heart failure refers to those individuals with structural heart disease but who remain asymptomatic from heart failure. Stage C thus reflects those individuals with structural heart disease who were previously or are currently symptomatic. Last, stage D heart failure reflects refractory heart failure despite appropriate therapy with an increased risk for recurrent hospitalization and death. Stage D requires specialized interventions for advanced therapy. Notably, the stages of heart failure are static categorizations and imply a unidirectional progression in disease. These stages differ from the dynamic New York Heart Association (NYHA) Functional Classification system, which relies on exercise capacity and current symptoms.[10]

Stages A and B Heart Failure

Ideally, heart failure management begins first with recognizing patients who have risk factors for heart failure, despite no apparent structural heart disease, also known as stage A heart failure. Management of stage A heart failure thus involves treating hypertension and hyperlipidemia according to contemporary guidelines in order to lower the risk for developing heart failure,[11,12] and, to a lesser degree, controlling obesity, diabetes mellitus, and tobacco use. Of these risk factors for heart failure, management of hypertension is the most important. Early work recognized the benefits of diuretics for hypertension treatment in preventing heart failure.[13,14] Recent data from the Systolic Blood Pressure Intervention Trial reinforcing this management strategy showed that intensive blood pressure control in those at higher cardiovascular disease risk treated with multiple agents to a goal systolic blood pressure $\leq$ 120 mm Hg led to a reduction in the composite primary outcome in nondiabetic, elderly patients and was primarily driven by a 37% reduction in the risk for nonfatal heart failure.[15] Replication of these results in younger populations would further establish effective hypertension management as a reasonable goal for stage A heart failure.

With the accumulation of risk factors for heart failure that could modify myocardial substrate, early use of noninvasive imaging, such as echocardiography, can help establish stage B heart failure, even before symptom development so that steps can be taken to ameliorate progression of disease and reduce mortality. Echocardiography in this case is commonly used to assess left ventricular dimensions, left ventricular hypertrophy, and calculation of ejection fraction. In the post–acute coronary syndrome or myocardial infarction setting, and left ventricular ejection fraction $\leq$40%, the Survival and Ventricular Enlargement and Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction trials showed relative reductions in mortality by 19% and 23% in individuals treated with captopril and carvedilol, respectively, versus placebo.[16,17] These studies paved the way for angiotensin-converting enzyme inhibitors (ACEI; angiotensin receptor blockers [ARB] if not tolerated), and evidence-based beta-blockers to be