Heart Failure and Hypertension

Importance of Prevention

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KEYWORDS

• Heart failure • Randomized clinical trials • Antihypertensive agents • Prevention

KEY POINTS

- Elevated blood pressure has the greatest population attributable risk for the development of heart failure.
- The mortality rates following the clinical recognition of heart failure is increased multifold.
- The treatment of hypertension with antihypertensive agents is particularly effective in preventing heart failure, which makes it the most effective therapy for heart failure.

Cumulative successes from randomized controlled clinical trials (RCTs) over the last 30 years in the treatment of patients with symptomatic heart failure with pharmacologic therapies as well as electrophysiological devices such as cardiac resynchronization therapy and autonomic implantable cardiac defibrillators have resulted in tangible improvements in prognosis.[1,2] These advancements are manifested by both an older age at which the first hospitalization for management of heart failure occurs as well as a lower rate of death following this initial hospitalization.[3] However, the RCTs that generated the evidence for these interventions that have favorably altered clinical practice, to date, have been entirely limited to the segment of the heart failure population with reduced ejection fraction (HFrEF). Those with symptomatic heart failure with a left ventricular ejection fraction (LVEF) that is only mildly impaired or even within the range considered normal (previously termed diastolic heart failure), now designated as heart failure with preserved ejection fraction (HFpEF), manifest the same signs and symptoms and have a similarly impaired quality of life.[4] These patients with HFpEF have only relatively recently been the focus of interventional clinical outcome RCTs. At present, none of the handful of RCTs targeting patients with HFpEF that were large enough to ascertain whether clinical outcomes can be altered has provided sufficiently robust evidence for an improvement in the prognosis for these patients.

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Once heart failure becomes manifested by signs and symptoms, the subsequent risk of death is generally increased by a factor of 5- to 10-fold compared with similar cohorts that do not develop clinical heart failure. This major detrimental impact of heart failure on lifespan can be readily demonstrated within epidemiologic cohorts as well as with RCTs. In broad representative community populations such as the Framingham Heart Study and Atherosclerosis Risk In Communities (ARIC), the mortality following clinical heart failure has been between 40% to 50% within 5 years of the initial diagnosis.[5,6] This multifold heightened risk for death following the clinical recognition of heart failure regardless of LVEF has been recapitulated within RCTs. For example, in clinical trials that excluded those with heart failure or conducted analyses of those without a prior history of this syndrome, the development of the signs and symptoms of heart failure had a clear multifold detrimental impact on longevity. In the Heart Outcomes Protection Evaluation (HOPE), which excluded those with heart failure as well as reduced ejection fraction, those manifesting heart failure had a much higher mortality than the remainder of the population even after adjusting for other pertinent differences (**Fig. 1**).[7] Similarly, in Cholesterol And Recurrent Events (CARE), an early statin trial in patients with coronary artery disease, 28% of the 243 patients who developed heart failure died in 3.5 years compared with 7% mortality within 5 years of the remaining 3617 patients.[8] In the Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints (ALTITUDE), hospitalization for heart failure was the most common initially nonfatal major cardiovascular event compared with myocardial infarction and stroke, and was associated with the near sixfold increased risk of death compared with those in the study who did not have an initial nonfatal event.[9]

The adverse impact of heart failure goes beyond shortened life span, as frequent exacerbations of signs and symptoms requiring hospitalization are a hallmark of the severe morbidity of this clinical syndrome. With therapeutic advancements, especially for heart failure with reduced ejection fraction, and with the shift in the population demographics with a larger number of those aged 65 years and older living with heart failure, the burden of this frequent disorder both individually and to society with increased health care utilization expenses, has continued to increase. Indeed, heart failure remains the leading cause for hospitalization in the Medicare population.[10,11] That the prevalence of heart failure continues to expand can be considered a reflection on the advances in treatments. However, the important observation of an older age at

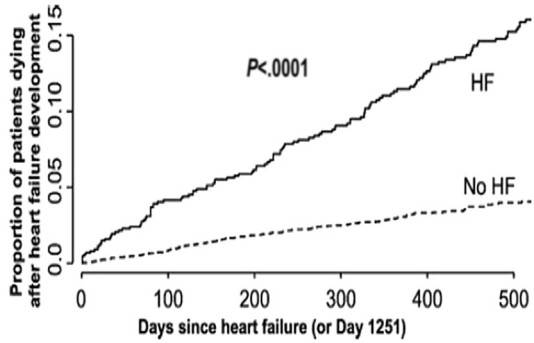

Fig. 1. Comparison of mortality rates between those who did and did not develop heart failure in the HOPE trial. (*From* Arnold JM, Yusuf S, Young J, et al. Prevention of heart failure in patients in the Heart Outcomes Prevention Evaluation (HOPE) Study. Circulation 2003;107:1285; with permission.)