Hypertension and Heart Failure
The ALLHAT Imperative

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Heart failure brings with it personal suffering and disability, lost productivity, and a growing burden on an already excessive US per capita medical care expenditure. As America’s baby-boom generation advances in age, we anticipate that the population band of people >65 years of age will swell significantly (Figure 1). Indeed, Census Bureau projections estimate that this number will rise from the current 40 million to 88 million by 2050. This census projection is especially worrisome when juxtaposed to a graph of the age of first heart failure events in a community population where the median age for incident heart failure was 80 years (Figure 2). Are we facing a tsunami of heart failure? You do the math. Is there reason for hope in the face of a tidal wave? Perhaps. A half-century of epidemiology has taught us much about the risk factors for heart failure, and clinical trials have provided evidence-based approaches to reduce the impact of those risk factors.

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Age may be the paramount risk factor for heart failure, but superimposed on age are modifiable antecedent clinical conditions: hypertension, atherosclerotic cardiovascular disease, diabetes mellitus, and obesity.¹⁻⁴ Framingham data show a lifetime risk for the development of heart failure of 20% in men and women.² Population-attributable risk estimates take into account the magnitude of a risk factor’s impact and its prevalence.³⁻⁵ Attributable risk estimates will vary, therefore, depending on the risk factor definition, the age of the cohort, and the method of ascertainment. Among women, hypertension accounted for 59% of heart failure in the Framingham data and 28% in Olmsted, MN. Corresponding figures for men were 39% and 13%. Hypertension and coronary disease are the most powerful heart failure risk factors in community studies. It is noteworthy that in women hypertension appears to be a greater risk than myocardial infarction, whereas in men myocardial infarction accounts for as much or more of the heart failure risk.

The systematic application of echocardiographic imaging techniques has clarified our understanding of the prevalence of left ventricular systolic and diastolic dysfunction and refined our appreciation of the role that ventricular dysfunction plays in the progression from heart failure risk factors to asymptomatic ventricular dysfunction, and from there to symptomatic heart failure and death.⁵⁻⁷ We now understand that 2.2% of the middle-aged and elderly patients have symptomatic heart failure as defined by the Framingham criteria, and that about half of these have preserved ejection fraction.³ But, in addition to these very symptomatic patients, there is an even larger group with clinically silent ventricular dysfunction. In a population-based community cohort of people ≥45 years of age, we have found that 6.0% have an ejection fraction <50%, and among those with a normal ejection fraction, 5.6% have moderate to severe diastolic dysfunction.⁵ For every person with heart failure, there are ≈5 persons with ventricular dysfunction who do not fulfill the Framingham criteria.

The American College of Cardiology/American Heart Association heart failure staging model was developed to emphasize the progressive nature of heart failure.⁸ Application of the American College of Cardiology/American Heart Association Heart Failure staging model to a randomly selected community population of people ≥45 years of age reveals that 22% of the population has stage A (heart failure risk factors without abnormalities of ventricular structure/function), 34% have stage B (abnormal ventricular structure/function without symptoms), 12% have stage C (abnormal ventricular structure/function with symptoms), and 0.2% have stage D heart failure (end stage).⁹ It is remarkable that 56% of the population has heart failure risk factors or asymptomatic ventricular dysfunction. Clearly, a large proportion of our middle-aged and elderly population is in need of medical attention to prevent clinical heart failure.

Hypertension Treatment and Heart Failure Prevention

For 40 years, data have accumulated suggesting that effective blood pressure control can reduce the risk of moving from stage A or B to stage C heart failure. In 1970, in a Veterans Administration trial of only 380 people with diastolic pressure 90 to 114 mm Hg, antihypertensive therapy reduced heart failure events from 2.6% of patients to 0.¹⁰ The Systolic Hypertension in Elderly Program (SHEP) trial included 4736 people ≥60 years of age and demonstrated that reducing blood pressure from 170/77 to 143/78 mm Hg reduced heart failure events by 48% (from 4.4% to 2.3%; relative risk=0.51, P<0.001).¹¹ In the Heart Outcomes Prevention Evaluation (HOPE) Study of 9297 patients with diabetes mellitus or vascular disease, ramipril was associated with a decrease in blood pressure from 139/79 to 136/76 mm Hg, and a 13% reduction in heart failure events (from 11.5% to 9.0%;
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), a landmark clinical trial in hypertension management, randomly assigned hypertensive patients with at least 1 other risk factor for coronary heart disease to treatment with chlorthalidone, lisinopril, or amlodipine. Between 1994 and 1998, some 33,357 patients were enrolled, 58% of whom were ≥65 years of age, a reduction of mean blood pressure from 173/91 to 144/78 mm Hg was associated with a 64% reduction in heart failure events (from 14.8% to 5.3%; relative risk=0.36, *P*<0.001). Although the magnitude of benefit varies with the trial selection criteria, target blood pressure reduction, and heart failure criteria, there is little doubt that effective hypertension treatment can reduce heart failure events.

Relative risk=0.77, *P*<0.001). More recently, in the Hypertension in the Very Elderly Trial (HYVET) of 3845 patients ≥80 years of age, a reduction of mean blood pressure from 173/91 to 144/78 mm Hg was associated with a 64% reduction in heart failure events (from 14.8% to 5.3%; relative risk=0.36, *P*<0.001). Although the magnitude of benefit varies with the trial selection criteria, target blood pressure reduction, and heart failure criteria, there is little doubt that effective hypertension treatment can reduce heart failure events.

Underscored, focused on persons at increased risk for the development of heart failure. Indeed, among these patients, who were being followed closely in a clinical trial to achieve hypertension control, 5.4% nevertheless experienced heart failure hospitalization or death. In this issue of *Circulation*, the ALLHAT investigators provide extended follow-up data. In the 1761 patients who were hospitalized for heart failure during the treatment phase of the trial, administrative databases (National Death Index, Social Security Administration, and *International Classification of Diseases, Tenth Revision* codes) were used to ascertain deaths due to heart failure and all-cause mortality through 2006. The mean total follow-up for this group was 8.9 years (4.9 years in the active treatment phase plus 4 years of posttrial follow-up).

Among these 1761 hypertensive patients hospitalized for heart failure, the authors report a 10-year all-cause mortality of ≈85%, with no significant differences between treatment groups and little difference between heart failure with reduced and preserved ejection fraction. Because there was no untreated control group, we cannot say how much mortality benefit hypertension treatment per se may have provided. We can say that the mortality in this elderly heart failure cohort is very high, and that if one follows patients long enough the relative benefits that may have been afforded by one of the treatment modalities eventually fades away, ie, if one waits long enough all mortality curves converge on 100%. We can also say that the 1761 hypertensive subjects who were hospitalized with heart failure during the trial are almost 3 times more likely to die (hazard ratio 2.89; 95% confidence interval, 2.69–3.11, *P*<0.001) during extended follow-up than hypertensive participants who were not hospitalized for heart failure. Furthermore, we learn that they were 8-fold more likely to incur a heart failure–related death (hazard ratio 8.06; 95% confidence interval 6.38–10.18, *P*<0.001). And, of course, we have no measure of the disability, economic stress, and pain these patients and their families endured.

ALLHAT is one of many trials showing that hypertension control can be achieved in most patients and, importantly, ALLHAT reminds us that widely available and inexpensive thiazide diuretics can be an effective means to that end. So, given that blood pressure control is feasible, how are we doing at it? The most recent National Health and Nutrition Examination Survey report indicates that we have much work to do. Overall, the US hypertension prevalence was 34%; among men and women ≥65 years of age, it was 64% to 79%. Although ≈80% of hypertensive patients >60 years of age are aware of their hypertension and are being treated, only half are being controlled (blood pressure, <140/90). There is cause for hope. Blood pressure control and lifestyle changes can have a significant impact. We have good tools, so the challenge is to apply them widely and consistently. Perhaps the most important statement the authors make is their conclusion that, "prevention of heart failure is a public health imperative." Their tone of urgency is warranted. The wave of heart failure is already upon us.

**Disclosures**

None.
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