

## Hypertension in the Elderly: An Under-Recognized Problem

*Based on a presentation by Alan B. Weder, MD*

### **Presentation Summary**

The elderly population bears a disproportionate share of cardiovascular disease in this country; in turn, isolated systolic hypertension accounts for the vast majority of hypertensive disease, and is the more important predictor or risk for cardiovascular disease in patients over the age of 65. Fortunately, the Systolic Hypertension in the Elderly Program (SHEP) trial and other studies have demonstrated that treatment of ISH effectively reverses much of the associated risk.

The progression of cardiovascular disease to congestive heart failure can follow two pathways: systolic dysfunction, resulting from a myocardial infarction (with hypertension, smoking, dyslipidemias, and diabetes as the key risk factors), or diastolic dysfunction, resulting from left ventricular hypertrophy

(with hypertension, obesity, and diabetes as the key risk factors). With systolic dysfunction, the heart cannot contract well enough to push out enough blood for the body's needs. Diastolic dysfunction, on the other hand, is defined by the absence of systolic dysfunction in the presence of symptoms of congestive heart failure, with normal or supranormal ejection fractions, small cavity sizes, and often left ventricular hypertrophy. It results from a failure of the heart to relax and fill properly during diastole. Some studies have suggested that diastolic dysfunction may be present in 30% to 40% of congestive heart failure patients. The two scenarios are treated differently; systolic dysfunction is treated primarily with inotropes and diuretics, while a variety of therapies are used in treating diastolic dysfunction.

**D**espite the concern in recent years over tragic diseases such as AIDS and cancer, cardiovascular disease remains the number one cause of death in this country, according to Alan B. Weder, MD, Professor of Medicine, University of Michigan, Ann Arbor, Michigan. He cited 1991 estimates from the National Center for Health Statistics, showing 860,000 deaths annually from cardiovascular disease, 150,000 of which can be attributed to stroke. "The elderly population bears a disproportionate share of cardiovascular disease in this country," he continued, accounting for 80% of the total

populational mortality and morbidity in the Framingham Heart Study.<sup>1</sup>

### **The Importance of Systolic Blood Pressure and Other Risk Factors**

Dr. Weder pointed out that "systolic hypertension is an increasingly important problem in the elderly"; isolated systolic hypertension (ISH) accounts for the vast majority of hypertensive disease at any given age over 65. Although diastolic hypertension does not disappear, it becomes much less predominant in the elderly population. Until recently, he added, ISH has been overlooked or regarded as a secondary problem, while

efforts have been focused on aggressive treatment of isolated diastolic and combined diastolic/systolic hypertension in younger patients.

Although it has been shown that increased diastolic blood pressure does contribute to cardiovascular risk, when combined with elevated systolic blood pressures (>160 mm Hg) it is much less of a risk factor than the systolic blood pressure. In fact, according to Dr. Weder, the major risk is associated with those elderly patients with ISH (systolic >160 mm Hg and diastolic <70 mm Hg), multiple concomitant disease, and the highest prevalence of both recognized and unrecognized coronary heart disease and congestive heart failure (CHF).

"We have tended to discount the importance of systolic blood pressure as a marker for risk in our patients," Dr. Weder remarked. However, there is little doubt from the epidemiologic literature and clinical trial data that systolic hypertension is the more important predictor of risk for those over age 60. "Fortunately," he said, "data from the SHEP (Systolic Hypertension in the Elderly Program) trial and others demonstrate that treatment of systolic hypertension effectively reverses much of the associated risk."

Dr. Weder also reviewed other risk factors for cardiovascular disease in the

elderly, including cholesterol, diabetes, and smoking. Hypercholesterolemia is also an age-related risk factor, he pointed out, although there is some fall-off in increased risk after age 65, probably due to competing mortalities. Glucose intolerance (a precursor to diabetes) also increases with age; even in a mild form, this represents an additional risk for atherogenesis. Interestingly, Dr. Weder noted, smoking rates actually decrease somewhat in the elderly, probably due to the extreme toxicity and mortality at younger ages with cigarette smoking.

"The evidence is unequivocal that we should be aggressively treating hypertensives," Dr. Weder asserted. A number of large trials have shown the benefit of treating hypertension; although most of these trials used beta-blockers and diuretics, there is no reason to think that these treatment effects are unique to those classes of drugs. In several trials, there were clear benefits of treating ISH, not only in reducing the risk of stroke, but also in reducing the risk of coronary artery disease, CHF, and overall cardiovascular disease (Table 1).

Dr. Weder contended that the evidence strongly points toward a continuity of risk at every level of blood pressure, which has redefined the goals of antihypertensive therapy. "The lower the blood pressure the better," he claimed, noting that we have gone from treating patients with systolic blood pressure above 160 mm Hg, to trying to treat systolic hypertension of 140 mm Hg.

### The Concomitants of Hypertension

Dr. Weder reviewed the progression of cardiovascular disease (Figure 1), noting that the presence of specific risk factors (smoking, dyslipidemia, diabetes) associated with hypertension greatly increases the risk for myocardial infarction (MI), especially in the elderly population. Left ventricular hypertrophy (LVH), once viewed as merely an interesting finding at autopsy, is clearly

**Table 1.** Reduction of Relative Cardiovascular Risk in Seven Major Trials

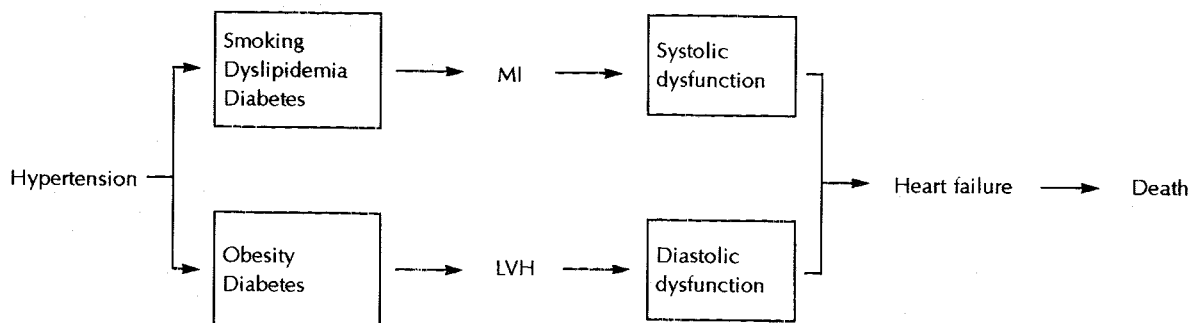
	Relative Risk in Treated Patients			
	Stroke	CAD	CHF	All CVD
Australian	0.67	0.82	-	0.69
EWPHE	0.64	0.80	0.78	0.71*
Coope & Warrender	0.58	1.03	0.68	0.76*
STOP-Hypertension	0.53*	0.87*	0.49*	0.60*
MRC	0.75*	0.81	-	0.83*
SHEP	0.67*	0.73*	0.45*	0.68*
HDFFP	0.56*	0.85*	-	0.84*

CAD = coronary artery disease; CHF = congestive heart failure; CVD = cardiovascular disease

\*Statistically significant compared with controls.

From the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: The fifth report. *Arch Intern Med* 1993;153:154-164.

**Figure 1.** Progression of Cardiovascular Disease



MI = myocardial infarction. LVH = left ventricular hypertrophy. From Levy D. In *The Role of Hypertension in Heart Failure* (slide kit) Merck & Company.

a cause of CHF, predominantly through diastolic dysfunction.

Long-term follow-up studies, such as the Framingham study, have shown that the risk of CHF increases markedly after an MI; interestingly, Dr. Weder noted, some patients with larger infarcts or anterior wall infarcts actually develop symptoms of CHF at the time of their MI. What is perhaps less obvious is that the incidence of CHF following an MI increases progressively with age<sup>2</sup>; this is due not to recurrent MIs or progressive loss of tissue, but to a complex phenomenon related to remodeling of the left ventricle. This remodeling, which is a "response to injury" following the original MI, actually promotes the development of CHF later on.

This high incidence of CHF following MI becomes important when one considers the 30% to 40% of elderly patients with unrecognized, undiagnosed MIs, as shown in serial electrocardiography (ECG) studies. These are probably a combination of silent ischemia and atypical chest pain presentations, which may be attributed incorrectly to gastrointestinal or other complaints. With this in mind, Dr. Weder cautioned, "we must be very suspicious in taking a history and

physical exam in elderly patients; a certain amount of screening with ECG in particular is reasonable in these patients."

### Systolic Dysfunction

Dr. Weder noted that CHF is "almost exclusively a disease of the elderly," mostly due to the time lapse between an MI (usually experienced in middle age) and the development of CHF. As Dr. Weder explained, what we have traditionally thought of as CHF is "basically poor pumping of the heart," due to systolic dysfunction, in which the heart cannot contract well enough to push out enough blood for the body's needs. Until recently, CHF has been regarded as a part of the aging process, and has been treated symptomatically with digoxin, diuretics, and ACE inhibitors. "We didn't really appreciate how serious a diagnosis this was," he added. In the Framingham study, almost 50% of men and 40% of women died within 1 year of presentation with CHF.<sup>3</sup> The 5- and 10-year survival rates for both men and women in this population were worse than those for many cancers in this age group. CHF, he pointed out, with its increasing incidence with age and the

rapid progression to disability and death, is one of the major reasons for hospitalization for the elderly and an increasingly prevalent cause of death in this country.

In the post-MI setting, clinical trials have shown a clear benefit of treating

*“Aging in and of itself does not usually present with symptoms of CHF, so we are dealing with a concomitant problem that aggravates that process, in this case LVH.”*

— Dr. Weder

the signs and symptoms of CHF. These trials, in the early 1990s, had to show a benefit over and above the optimized treatment of post-MI patients with aspirin and beta-blockers. Based on the results with animal studies, angiotensin converting enzyme (ACE) inhibitor therapy was studied in several trials. In the Survival and Ventricular Enlargement (SAVE) trial, in asymptomatic post-MI patients with an ejection fraction (<40%, treatment with captopril resulted in a 21% risk reduction ( $P = 0.014$ ) compared with placebo.<sup>4</sup> In this trial as in others, “the sparing of mortality actually occurs late, after about 2 years, well after the acute effects of the MI,” Dr. Weder commented. By treating post-MI patients, we are “not simply taking care of the infarcted heart and preserving myocardium in the first couple of days after the MI, but actually preventing a long-term process (the response to injury and subsequent remodeling) that ultimately is harmful.” He added that this late sparing of mortality may indicate a benefit of ACE inhibitor treatment on atherosclerosis and coronary artery disease; several large trials are currently under way to address this question.

Two other trials, with ramipril and enalapril, also showed similar benefits, indicating that “this is probably a class effect,” Dr. Weder reported. The Acute

Infarction Ramipril Efficacy (AIRE) Study showed a relative hazard of 0.73 for patients treated with ramipril at 1 year compared with placebo ( $P = 0.002$ ),<sup>5</sup> while the Studies of Left Ventricular Dysfunction (SOLVD) trial showed a 20% risk reduction ( $P = 0.0045$ ) in post-MI patients with ejection fractions of 35% or less treated with enalapril.<sup>6</sup>

Dr. Weder also discussed the prevention limb of the SOLVD trial, in which ACE inhibitor therapy was associated with an 83% reduction in ischemic heart disease, an 80% reduction in MIs, a 37% reduction in hypertension, and a 34% reduction in symptoms of angina. Most importantly, in these New York Heart Association class I-II patients, with LVD as documented on echocardiography and ejection fractions below 35%, ACE inhibitor therapy resulted in a 32% reduction in symptomatic CHF, with a similar reduction in hospitalization rates. “A one-third reduction in hospitalization for the number one cardiovascular cause of hospitalization should justify use of this relatively benign and reasonably well tolerated intervention, even with the additional testing (eg, echocardiography) that will be required,” he concluded.

#### Diastolic Dysfunction

As Dr. Weder explained, “diastolic dysfunction is defined by and large by the absence of systolic dysfunction in the presence of symptoms of CHF.” Ejection fractions—either with nuclide studies or echocardiography—tend to be normal or above normal. Patients usually have small cavity sizes, often associated with LVH. The problem in diastolic dysfunction, Dr. Weder said, “really comes from a failure of the heart to relax and fill properly during diastole.” Clinically, these patients are identical in presentation to those with systolic dysfunction, with indistinguishable symptoms such as pulmonary venous congestion and dyspnea. Diastolic dysfunction can be thought of as a normal problem of aging; however, he added, “aging in and of itself does not

usually present with symptoms of CHF, so we are dealing with a concomitant problem that aggravates that process, in this case LVH.”

LVH is an extremely common concomitant of aging, particularly in women, he continued. “These massively hypertrophied hearts, with very small cavity sizes, are very muscular,” with normal to supernormal ejection fractions. “The problem is relaxing and filling; if one stresses this heart by increasing the heart rate and compromising diastolic filling time, you can get into trouble in a hurry.”

Diastolic dysfunction is diagnosed by a combination of echocardiography (to determine muscle mass) and Doppler studies. In Doppler studies of the normal heart, flow through the mitral valve during diastole is usually biphasic. The early phase is characterized by an E wave, in which the left ventricle relaxes and is filled passively; this is followed by a period of diastasis, and then an A wave, resulting in atrial contraction. In the normal heart, most of the filling is accomplished during the early phase of passive filling. In the hypertrophied or ischemic heart, this pattern is often reversed, Dr. Weder noted. As the heart stiffens, passive filling becomes more difficult. To maintain cardiac output and left ventricular filling, the A wave component is increased, with greater atrial contraction. The atrium actually hypertrophies to some degree, and normal hemodynamics are maintained by increasing the contribution of atrial filling. Once this is at a maximum, left ventricular diastolic pressure and left atrial pressure must be increased to maintain left ventricular filling. “Eventually, if you increase these pressures enough, you will back up into the lung and develop symptoms of CHF,” he concluded.

Although this was once thought to be an uncommon scenario, some studies have suggested that 30% to 40% of patients with CHF have normal ejection fractions, and therefore diastolic dysfunction.<sup>7</sup> This may be an overestimate,

Dr. Weder pointed out, since some of these patients may have had systolic dysfunction that resolved prior to examination, eg, from acute ischemia.

**Table 2.** Treatment of CHF Caused Primarily by Diastolic Dysfunction

Treatment Goal	Therapy
Decrease venous pressure	Diuretics, nitrates
Prevent/decrease LVH	Decrease blood pressure, repair aortic valve
Prevent/treat ischemia	Beta-blockers, calcium entry blockers, nitrates
Decrease heart rate	Beta-blockers, calcium entry blockers
Maintain atrial contractility	Cardioversion, atrial fibrillation, sequential atrioventricular pacing

NOTE: Avoid potent direct-acting arterial vasodilators

From Cupples.<sup>2</sup>

Since systolic and diastolic dysfunction cannot be distinguished based on symptomatology, echocardiography is a reasonable technology for determining the etiology.

This is necessary, he continued, because systolic and diastolic dysfunction are treated differently. “Whereas we typically treat systolic dysfunction with inotropes and diuretics, we need to use these drugs much more cautiously in diastolic dysfunction.” A variety of therapies have been used to treat diastolic dysfunction (Table 2); the challenge is to adjust medications to improve the symptoms, including preventing or reducing LVH during the treatment of hypertension and repair of any valvular abnormalities. “If you can reduce LVH back to normal,” Dr. Weder commented, “often diastolic dysfunction remits at the same time.” For this reason, treatment of hypertension should also address the prevention and reversal of LVH.

### Conclusion

As Dr. Weder concluded, “there are really two kinds of heart disease in the

elderly." The first is coronary artery disease, and "we may not appreciate how often and how rapidly this leads to CHF, and how rapidly CHF leads to death." The second is LVH, a precursor to diastolic dysfunction and CHF. However, he stressed, "if we treat the hypertension, we can prevent any of this from happening in the first place."

... REFERENCES ...

1. Bierman EL. Aging and atherosclerosis. In: Hazard WR, Bierman EL, et al, eds. *Principles of Geriatric Medicine*. 3rd ed. New York, NY: McGraw-Hill; 1994:509-516.
2. Cupples LA, D'Agostino RB. In: Kannel WB, Wolf PA, Garrison RJ, eds. *The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease*. Washington, DC: US Government Printing Office; 1987. DHHS publication NIH 87-2703; section 35.
3. Ho KKL, Anderson KM, Kannel WB, et al. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation*. 1993;88:107-115.
4. Pfeffer MA, Braunwald E, Moya LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: Results of the Survival and Ventricular Enlargement Trial. *N Engl J Med*. 1992;327:669-677.
5. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. *Lancet* 1993;342:821-838.
6. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293-302.
7. Soufer R, Wohlgeleitner D, Vita NA, et al. Intact systolic left ventricular function in clinical congestive heart failure. *Am J Cardiol* 1985;55:1032-1036.