Seniors and Systolic Hypertension

An Unanswered Call to Arms

Over half a century of research in hypertension therapy, an explosive growth in antihypertensive medications, and a marked increase in awareness of the complications of uncontrolled hypertension have not been matched by progressively improving hypertension control rates in the United States or worldwide. Rates of controlled hypertension (BP, < 140/90 mm Hg) range from a high of 27% (1994 US National Health and Nutrition Examination Study III) to a low among European countries of approximately 6% (in the United Kingdom). Elderly patients with isolated systolic hypertension (systolic BP, > 140 mm Hg; diastolic BP, < 90 mm Hg) are the demographic group least likely to have their BP controlled. Forty-one percent of all people > 65 years of age and 65% of African Americans > 65 years of age have uncontrolled systolic hypertension. This is particularly important as systolic BP is a better predictor of events such as coronary heart disease, stroke, congestive heart failure, renal failure, and all-cause mortality than is diastolic BP. Despite clear evidence of the marked increase in cardiovascular morbidity and mortality associated with poorly controlled systolic hypertension and consistent data from trials on the many benefits of lowering BP, changes in physician and patient behavior that would result in improved BP control have not occurred. Why haven’t rates of control of systolic BP improved? Multiple factors need to be considered.

The first area to be addressed is physician practice. Recent results from the Systolic Hypertension in the Elderly (SHEILD) survey showed that while 77% of physician respondents were aware of the guidelines for hypertension management in the 1997 Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI), the survey reports a far lower awareness among family and general practitioners (38%). General practitioners (30%) and internists (38%) were less likely to consider treating systolic hypertension to goal level than were cardiologists (58%). Why would those physicians most involved in the management of hypertension be less inclined to aggressively treat systolic hypertension in the elderly? There are several considerations. One of the dominant issues is the rapid change in guidelines for managing isolated systolic hypertension. The 1984 Joint National Committee (JNC) guidelines for the treatment of hypertension in the elderly were based on limited numbers of patients > 60 years of age. They warn that if this is not done, overdiagnosis bias, like the gyanousa, might escape its cage and run amok.

But physicians are not rubes, and, hopefully, specialists in radiology, pulmonary medicine, and thoracic surgery are not benighted yokels. We must not be induced to flee in terror of phantoms. No one has ever actually seen a gyanousa, and precious few cases of overdiagnosed lung cancer have ever been observed or reported. Both are mythical beasts. The first, the gyanousa, is a concoction of hucksters. The second, lung cancer overdiagnosis bias, is a preposterous product of the overactive imaginations of a group of theoretician epidemiologists at the NCI and elsewhere who have little clinical experience caring for the victims of the real monster, lung cancer. And make no mistake; lung cancer is a true monster, and it really is loose, a ravening beast that consumes 160,000 people in our country each year. We should be hot on the track of this very real and deadly killer and run amok.

References

age in the Veterans Administration cooperative study, the Hypertension Detection and Follow-up Program study, the Australian Therapeutic Trial, and the one large trial designed to treat hypertension in the elderly, the European Working Party Trial. This led to the following very conservative statement: “When the systolic BP is consistently > 160 mm Hg, despite nonpharmacologic therapy, drug therapy should be considered on an individual basis.”9 Little change occurred with the 1988 JNC guidelines, which stated the following: “For most elderly patients with isolated systolic hypertension, nonpharmacologic therapy seems warranted. If the decision is made to treat with drugs, systolic BP should be lowered cautiously (author’s emphasis) to the goal of 140 to 160 mm Hg.”10 Thus, as we entered the 1990s, the primary-care physician did not feel a sense of urgency about the treatment of systolic hypertension in the elderly. Trial data from the 1990s devolved to the latest JNC VI evidenced-based guidelines (author’s emphasis). The results of the Systolic Hypertension in the Elderly (SHEP) trial, the Hypertension Optimal Treatment (HOT) trial, the Swedish Trial in Old Patients with Hypertension (STOP)-2 study, and the Systolic Hypertension in Europe (Syst-Eur) trial led to dramatic change. “The goal of treatment in older patients (systolic BP > 160 mm Hg) should be the same as in younger patients (to below 140/90 if at all possible)[author’s emphasis], although an interim goal of [systolic] BP < 160 mm Hg may be necessary in those patients with marked systolic hypertension.”15 It is clear that in a time of multiple changing guidelines, further education of all physicians, especially those in primary care, is needed to modify practice behavior regarding the management of systolic hypertension in the elderly.

A second issue that interferes with control of systolic BP is concern about the side effects of BP medication, particularly orthostatic hypotension. In the SHIELD survey, physicians expressed concern about the efficacy and tolerability of medications in the elderly despite the fact that the SHEP trial, the STOP-2 trial, and the Syst-Eur trial have proven that antihypertensive medications are well-tolerated in the elderly who participate in trials. The HOT study had greater success achieving study BP targets among older patients compared to younger patients, with similar, low incidences of medication side effects in both groups. The variety of different classes of agents available for hypertension therapy makes it increasingly likely that an agent can be found that will lower systolic BP in an individual patient without remarkable side effects. Others have argued that this increasingly diverse array of antihypertensive agents, coupled with patients with multiple medical problems and pressures on the physician to spend less time with the individual patient, leads to worse BP control.17 On the other hand, rational combinations of drugs lead to better adherence, less complex regimens, and better control of BP. Finally, the Syst-Eur trial, like many other trials, has shown that reaching the goal level for systolic BP often requires more than a single antihypertensive agent.14 The increasing number of products for hypertension treatment reflects the observation that successful control of hypertension is directly related to the number of pills that need to be taken that combine two BP-lowering drugs in a single pill.

A third issue is the loss of focus on the importance of systolic BP because of the continued flow of new information about hypertension management. The recent recognition of pulse pressure as a determinant of cardiovascular outcome may, to the primary-care physician, be a source of confusion rather than clarification of what constitutes successful BP control. The Heart Outcomes Prevention Evaluation trial demonstrated increased cardiovascular benefit from the use of the angiotensin-converting enzyme (ACE) inhibitor ramipril to a degree greater than would be expected from the very modest additional lowering of BP in people > 50 years of age. This perceived benefit of ramipril might distract the physician from the imperative to further lower systolic BP. This is similar to the usage of ACE inhibitors in diabetic nephropathy in that there may be acceptance by the patient and the physician of only a partial reduction of systolic BP as a therapeutic success. An alternative hypothesis is that this failure to achieve BP goals is reflective of a reduction in the time spent with each individual patient coupled with an increasingly complex patient population in the current medical climate.

Many of the elderly have other comorbid diseases such as diabetes, coronary artery disease, congestive heart failure, and renal failure that further influence the choice of antihypertensive agent and the goal level for systolic BP. In diabetes and nonproteinuric renal disease, the goal for BP is < 130/85 mm Hg. In renal disease with proteinuria of > 1 g/24 h, the goal for BP is 125/75 mm Hg. In all three diseases, ACE inhibitors are to be preferred when constructing the antihypertensive regimen, but the initial use of an ACE inhibitor is not a substitute for eventually reaching the goal for the systolic BP level.

It is important to consider the impact of achieving BP goal levels in older persons. Multiple studies have validated the improvement in renal survival found in the captopril study in diabetes. Successful BP control with an ACE inhibitor can markedly delay the progression of renal failure in patients with proteinuric renal disease, allowing an older patient with diabetes to live a fuller life unencumbered by dialysis therapy. Likewise, BP control in the SHEP
The STOP-2 trial, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) have shown dramatic reductions (approximately 50%) in the development of congestive heart failure in the elderly. Congestive heart failure is the leading reason for an admission to the hospital among older persons and often is a prelude to the end of independent living for these patients. Finally, there is increasing interest in the ability of BP control to reduce the onset of dementia. Studies have shown a correlation between systolic BP and MRI quantification of small-vessel disease in the brain. Preliminary data have shown a preservation in cognitive function to be associated with a reduction in systolic BP. In older patients, we need to emphasize the power of good control of systolic BP to reduce dialysis, dementia, and debilitating hospitalization for congestive heart failure for patients well into their eighties. This improved quality of life, more than the mortality statistics for elevated systolic BP, may have an impact on the seniors and on their desire to have their BP controlled. Clearly, our current educational efforts, based mainly on reduction in mortality, have been less than successful in changing the behavior of our older patients and their physicians. As William Wordsworth has said: “O Death, where is thy sting?”

How can we improve control rates of systolic BP in the elderly? First, we need to emphasize a protocol-driven, relentless pursuit of the JNC VI guidelines for control of systolic BP. We have shown that a nurse-physician model of BP management using a protocol-driven approach can achieve control rates in older patients for systolic and diastolic BP similar to the 50 to 60% success rates seen in the major trials of hypertension, such as ALLHAT. Similar results have been seen from the International Verapamil Trandolapril study in elderly patients, using an Internet-based protocol approach and resulting in 53% of patients with BPs of <140/90 mm Hg after 2 years of the trial. Although this rate is better than the current overall control rate in the United States (27%), it still leaves far too many seniors at risk for morbidity from hypertension, so further strategies must be considered. Educational efforts redirected at the message of reduction of disability may be more effective in persuading seniors to be active partners in the pursuit of successful BP reduction. Increased utilization of a rational combination of antihypertensive agents represents a return to an old idea that may be extremely beneficial in treating hypertension in the elderly. Because adherence is directly related to the number of antihypertensive agents needed to control BP, combination products (i.e., diuretics with β-blockers, ACE inhibitors, angiotensin II receptor blockers, and calcium channel blockers with ACE inhibitors) may be of great help to older patients who are already burdened by multiple medications for their diabetes, degenerative arthritis, or heart disease. Studies have shown that seniors are more likely than younger patients to want to adhere to therapy, but they require help in developing a system that would incorporate the many medications they require and would avoid not only missed doses but drug-drug interactions. Most medication errors in hospitals are systems mistakes, not intentional errors, and seniors with multiple medications offer an opportunity to utilize the information technology explosion. Home BP monitors are available that can download the recorded BPs by modem to a central source and allow for real-time determination of individual and group control rates. Continuous feedback on BP control derived from out-of-office BP measurements has been shown to reduce the cost of care of hypertension. The rapid titration of antihypertensive medications to achieve goal levels for BP has been shown to be possible and not fraught with medication side effects, such as orthostatic hypotension, as was previously thought. On the horizon are newer medications that may have great efficacy in the reduction of systolic BP. Omapatrilat, representing a new antihypertensive class (vasopeptidase) and combining ACE inhibition with the inhibition of neutral endopeptidase in a designer molecule, has been shown to cause a far greater reduction in systolic BP (26.3 mm Hg vs 17.2 mm Hg) than that seen with the angiotensin II receptor blocker losartan.

The National High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute has issued two clinical advisories this year emphasizing the importance of reducing systolic BP and the lower treatment goals for diabetic patients. It is time to redouble our efforts for the reduction of systolic BP, especially among seniors. The successful reduction of systolic BP reduces the risk of congestive heart failure, end-stage renal disease, and dementia with even greater benefits in diabetic patients. This produces not only an increased chance of the elderly enjoying the “golden years” unencumbered by debilitating health concerns but also a reduction in the cost of health care. The array of antihypertensive medications available provides the physician with the means to control systolic BP. We also have the information technology necessary to improve the management of a chronic disease such as hypertension. Data on the control rates of systolic BP can be compiled readily, which permits an objective measure of the success of health-care providers in treating systolic hypertension. The first report on BP control rates in health maintenance organizations compiled by the National Committee for Quality Assurance indicates
a range of 28 to 48% for the treatment of hypertension. Of the chronic, high-cost medical illnesses, only diabetes and hypertension management can easily be graded objectively and have deficiencies promptly corrected. A public re-stating of the importance of the reduction of systolic hypertension combined with a structured protocol-driven approach to the reduction of systolic BP will improve the numbers of patients who achieve their goal BP level. Excellence of care and improved patient outcomes are always the best cost-saving measures available in medicine today.

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What Outcomes Should Be Measured in Patients With COPD?

Traditionally, pulmonary physicians rely on measures of lung function to diagnose, to assess disease severity, and to determine response to therapy in patients with COPD. The FEV₁ has been used as the main outcome in many clinical studies. Survival has been the main end point in several clinical trials for COPD, but only a few interventions (eg, administration of supplemental oxygen to hypoxemic patients) have been demonstrated to improve survival. However, the bulk of therapy for COPD has been aimed at improving quality of life. Many clinical studies of patients with COPD have not used quality-of-life measures as outcomes.

Quality of life has been defined in many ways, such as “the gap between that which is desired in life and the extent to which this is achieved or achievable.”1 The term health-related quality of life (HRQL) reflects the health- and disease-related aspects of quality of life. HRQL measurements quantify the impact of disease, treatments, and tests on daily life and well-being in a formal and standardized way.

As patients become symptomatic from COPD, the most common complaints are breathlessness, fatigue, sleep disturbances, irritability, and a sense of hopelessness. Dyspnea typically leads to inactivity, which leads to physical deconditioning, and a vicious cycle ensues, with devastating responses such as depression. Although a relationship between dyspnea and measures of lung function may exist,1-5 no single physiologic measurement (eg, FEV₁) can adequately encompass the various disturbances that cause dyspnea in patients with COPD. Direct measurement of dyspnea and other areas of HRQL may provide better estimates of the impact of disease and treatment effects than measurement of physiologic variables.

FEV₁ has been utilized as a surrogate marker of dyspnea and generic HRQL. However, pulmonary rehabilitation trials have demonstrated improvements in dyspnea without significant accompanying changes in parameters of lung function, including FEV₁.6 In addition, use of surrogate markers as primary outcomes in treatment trials can be dangerous. Many technologies that succeeded in improving surrogate markers failed miserably for the patients. For example, the Coronary Arrhythmia Suppression Trial7 randomized patients with recent myocardial infarction to receive different anti-arrhythmic agents, including encainide and flecainide, to treat premature ventricular contractions (PVCs). The investigators hypothesized that PVC suppression would reduce the triggers responsible for initiating a sustained ventricular tachyarrhythmia and thus reduce the incidence of sudden death. Although the occurrence of low-grade arrhythmias did decrease dramatically, the study was terminated prematurely because patients who were given encainide or flecainide had greater mortality rates than those receiving placebo therapy. The surrogate markers were not tightly linked to the more important patient outcomes.

Once we decide to measure HRQL, what tools do we use? Researchers often classify HRQL instruments as disease-specific or generic. Preference-based HRQL measures are typically classified as a separate group.

Disease-specific measures focus on the symptoms of the specific disease, such as shortness of breath. Generic measures provide information about many aspects of patients’ lives. Compared with generic measures, disease-specific measures may be more sensitive, because a much higher proportion of their content is directly relevant to a specific disease (eg, emphysema). In addition, disease-specific measures are likely to be more responsive (eg, able to detect small but clinically important changes in health status) because they focus on the symptoms of the specific disease. Unlike generic measures, disease-specific measures are limited by their noncomprehensive approach and their inability to compare status across diseases. Examples of instruments specific to lung-disease include the St. George’s Respiratory Questionnaire, the Chronic Respiratory Questionnaire, the Oxygen Cost Diagram, the Baseline and Transitional Dyspnea Indexes, the Modified Med-