The Diastolic Blood Pressure in Systolic Hypertension

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Because antihypertensive therapy is effective in elderly patients with isolated systolic hypertension, attention has been focused on the systolic blood pressure as a predictor of cardiovascular risk. However, it is a normal diastolic pressure that separates patients with isolated systolic hypertension from those with essential hypertension. The normal diastolic and elevated systolic pressures are largely due to age-related stiffening of the aorta. An indistensible aorta causes the pressure pulse to travel faster than normal, where it is quickly reflected off the peripheral resistance. The reflected wave then returns to the central aorta in systole rather than diastole. This augments the systolic pressure further, increasing cardiac work while reducing the diastolic pressure, on which coronary flow is dependent. The potential harm of further reducing the diastolic pressure with antihypertensive therapy, especially in patients with coronary heart disease, underlies the controversial "J curve." By decreasing the blood pressure, all antihypertensive agents improve aortic distensibility, but no agents do so directly; the nitrates come the closest. Such an agent would be useful because any therapeutic increase in aortic distensibility would decrease systolic pressure without greatly reducing diastolic pressure. The problem is complicated by the suspected inaccuracy of the cuff technique in predicting the aortic diastolic pressure. New noninvasive methods to predict the aortic diastolic pressure may help in the future. At present, the combination of a high systolic and normal diastolic pressure—a widened pulse pressure—seems to be the best predictor of cardiovascular risk in patients with hypertension or heart disease. Patients with isolated systolic hypertension should be treated, but marked diastolic hypotension should be avoided.

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The prevalence of isolated systolic hypertension increases with advancing age, and it is now estimated that 20% of persons 75 years of age are affected (1). Therefore, as the population ages, the number of patients with the disorder will rise, making it an increasingly frequent clinical problem. For obvious reasons, emphasis has been placed on systolic blood pressure in isolated systolic hypertension, but consideration of the diastolic blood pressure may offer greater insight into the disease.

In 1927, Fineberg (2) first divided hypertensive patients into systolic and diastolic groups. Over the ensuing years, opinions about what is now called isolated systolic hypertension have changed markedly. Initially, it was considered a nondisease, a natural consequence of aging that was unworthy of therapy. Later, it was shown to have an associated mortality rate higher than that among persons of the same age without elevation of systolic blood pressure (3, 4). At that time, conventional wisdom held that antihypertensive treatment in patients with isolated systolic hypertension was risky because reducing the systolic blood pressure might induce stroke in patients who also had subclinical cerebrovascular disease (5). These fears were allayed by the findings of the Systolic Hypertension in the Elderly Program (SHEP) study (6) and Systolic Hypertension in Europe Trial (7), which showed unequivocal benefit from decreasing the blood pressure in patients with isolated systolic hypertension by using hydrochlorothiazide or the long-acting calcium-channel antagonist nitrendipine. Since the publication of the reports of these trials, attention has been largely directed to the systolic blood pressure. However, far less has been written about the normal or low diastolic blood pressure that separates patients with isolated systolic hypertension from those with essential hypertension.

The first issue is whether the cuff method for measuring the diastolic blood pressure is accurate in patients with isolated systolic hypertension. Although considerable scatter always results when cuff pressures are compared with intra-arterial brachial artery pressures, no systematic error has been found in comparisons of systolic blood pressure (8). By contrast, when disappearance of the Korotkoff sounds (phase V) is used, cuff diastolic pressures are consistently higher than intra-arterial pressures

by 10 to 15 mm Hg in patients with isolated systolic hypertension, those with peripheral atherosclerosis, and elderly persons (8–10). Therefore, the intra-arterial brachial artery diastolic pressures are even lower than the "normal or low" values used as entry criteria for recent studies of isolated systolic hypertension.

An even more vexing question is how well cuff pressures represent central aortic pressures, against which the heart must pump in systole and on which the coronary flow depends in diastole. Direct comparisons of cuff brachial artery pressures with those of the ascending aorta have not been made in patients with isolated systolic hypertension and would be difficult in this group because of the necessarily invasive nature of direct aortic pressure measurements. Other techniques for indirect measurement of aortic pressure are available, such as applanation of the carotid artery (11) or transfer functions from the carotid or even a more peripheral artery (12, 13), but the accuracy of these methods might still be in question among patients with isolated systolic hypertension because of the variability in the measurements and the inhomogeneous changes in the arterial walls that occur with aging.

Because most patients with isolated systolic hypertension are elderly and because the central aorta is known to stiffen with aging, the indistensible aorta provides a ready explanation for the high systolic blood pressure and low diastolic blood pressure in such patients (14). When the aorta is noncompliant, it is less able to stretch and accommodates even a normal stroke volume with a higher systolic blood pressure. As a consequence, more of the stroke volume is forced into the periphery during systole, leaving less blood in the arterial tree during diastole, which accounts for the lower diastolic blood pressure.

Another governing principle is that pressure waves travel faster through stiff pipes than through pliant ones. Therefore, pulse-wave velocity is faster in older persons, in whom the aorta is stiffer, than in younger persons. In both younger and older persons, these pressure waves are reflected off the peripheral resistance, which for the lower body can be localized to the level of the renal arteries (15). In younger persons, the waves that travel more slowly reach the reflecting sites and return to the central aorta at the end of systole or early diastole, at which point they amplify the mean diastolic pressure. Because the distance is shorter, reflections from the upper body reach the aorta first. With aging, reflected waves from the upper and especially the lower body travel faster and return to the central aorta in early to mid-systole, where they augment the already elevated systolic blood pressure and increase the work of the heart (16). These reflected waves are the major cause of elevated systolic blood pressure, and thus the pulse pressure, in elderly persons. The amplitude of these wave reflections is even greater in hypertensive patients with elevated vascular resistance, the primary hemodynamic abnormality in essential hypertension. Loss of the reflected pulse augmentation in diastole reduces the mean diastolic pressure, the driving pressure for the coronary circulation, but has little effect on the minimal diastolic pressure recorded by the cuff method. These variations in aortic pulse wave shape were first described by Murgo and colleagues in 1980 (17). The pathophysiologic sequence of reduction in aortic distensibility is summarized and illustrated in the **Figure** in a pulse diagram (18).

The mechanisms described may account for the high prevalence of isolated systolic hypertension in elderly persons, but they fail to account for older persons who do not have the disease. Individual variations in the severity of aortic stiffening may be due to biological variability, environmental factors (19), or genetic factors (20). Accurate measurements of aortic distensibility are available (21, 22) and would help determine which patients have stiff aortas, but the studies are invasive and are not easily applicable to persons with isolated systolic hypertension. Further complicating the issue is that as a viscoelastic structure, the aorta stiffens with blood pressure elevation from any cause. Put another way, a stiff aorta could be the cause of systolic hypertension, the effect of essential hypertension, or both, and future measurements of aortic distensibility in isolated systolic hypertension will have to take the blood pressure itself into account as a variable.

The contribution of atherosclerosis to the aortic stiffening found with aging is easy to separate out in concept but is difficult in practice. In terms of hemodynamics, early atherosclerosis is a disorder of the arterial intima that has little effect on wall properties. However, aging stiffens the media, producing the pathological changes described above. Widespread, severe aortic atherosclerosis undoubtedly contributes to the loss of aortic distensibility to an undefinable extent when it coexists with the aging process. On the other hand, the medial stiffening found with aging probably plays little role in the genesis of atherosclerosis.

Even in the absence of atherosclerosis, other factors may influence the blood pressure in persons with a stiff aorta. Some patients with isolated systolic hypertension have high systemic vascular resistance, whereas others have a high stroke volume (23, 24), but neither of these conditions reduces the diastolic blood pressure. It is therefore likely that lack of aortic pliability is necessary but not always sufficient for the development of isolated systolic hypertension.

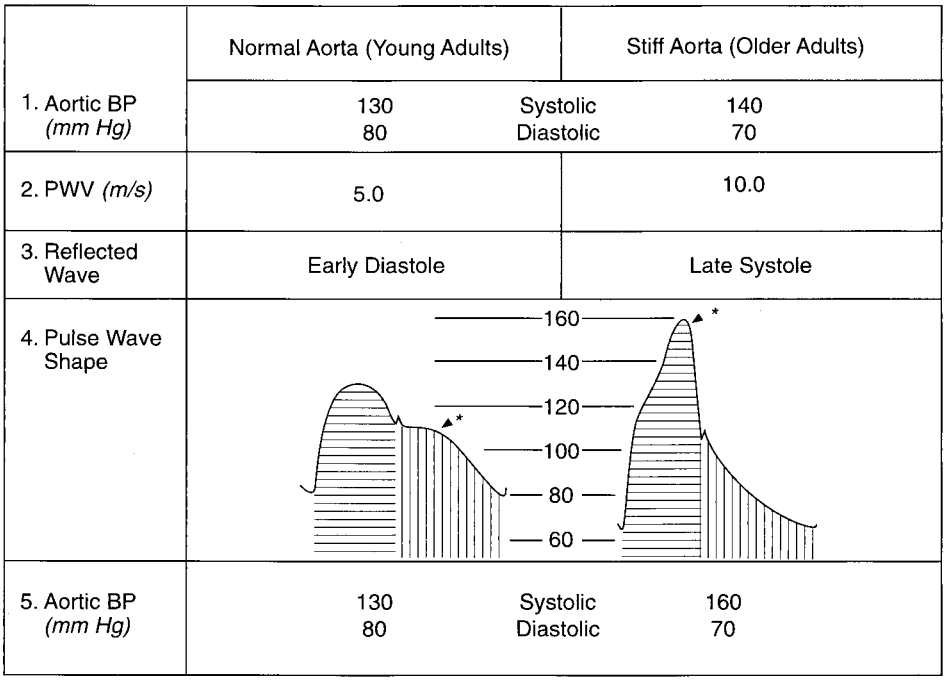

Figure. Development of aortic pressure abnormalities due to age-related aortic stiffening. 1. Increased systolic blood pressure (*BP*) and decreased diastolic blood pressure due to decreased aortic distensibility. **2.** Increased pulse wave velocity (*PWV*) as a result of decreased aortic distensibility. **3.** Return of the reflected primary pulse to the central aorta in systole rather than diastole because of faster wave travel. **4.** Change in the shape of the pulse wave because of early wave reflection. Note the reduction in diastolic pressure-time despite the increase in systolic pressure. Horizontal lines indicate systole; vertical lines indicate diastole. **5.** The aortic blood pressure resulting from decreased aortic distensibility and early reflected waves. * Primary reflected wave. Adapted from reference 18; pulse calibrations added by the authors.

High systolic blood pressure seems to be an obvious risk factor for stroke, increased left ventricular mass, and congestive heart failure. Whereas the mean blood pressure is the driving pressure for all other vascular beds, the diastolic blood pressure primarily drives the coronary flow. A low diastolic blood pressure, especially in the presence of coronary artery disease, may therefore explain the "J-curve phenomenon." The J curve has been described as an increasing cardiovascular risk when the cuff diastolic blood pressure is decreased by using antihypertensive therapy to less than 80 to 85 mm Hg (25–27). The expected decrease in diastolic blood pressure induced by therapy could be even greater in elderly persons with a stiff aorta and, as discussed previously in this paper, the aortic diastolic blood pressure may be even lower than that measured by the cuff method.

It is interesting that the initial fear of reducing the systolic blood pressure in patients with isolated systolic hypertension has proved to be unfounded, but our present concern may instead be excessive reduction of the diastolic blood pressure. The J-curve may be a bugaboo; it has not been found in a detailed retrospective observational study or a drug trial (28, 29). The drug trial, however, included only patients with diastolic hypertension (≥90 mm Hg) whose average diastolic pressures decreased by only 5 to 6 mm Hg. The J curve was not discussed in either the SHEP study or the Systolic Hypertension in Europe Trial, in which the diastolic blood pressure was clearly reduced to approximately the same extent. In a follow-up to the SHEP trial, no evidence of a J curve was detected (30). However, in a recent reanalysis of the SHEP data, a dose–response relation was seen in treated patients for more cardiovascular disease as the diastolic blood pressure decreased to less than 70 mm Hg (31). Nonetheless, the potential risk associated with a low diastolic blood pressure did not outweigh the favorable effects of reducing the systolic blood pressure.

The recently published Hypertension Optimal Treatment randomized trial (32) sought to identify the J curve but included only patients with elevations of diastolic blood pressure, and the results are therefore not applicable to patients with isolated systolic hypertension. Nonetheless, the results of the Hypertension Optimal Treatment trial regarding the J curve were equivocal; an observed increase in cardiovascular mortality with diastolic blood pressures less than 86 mm Hg was suggestive but not statistically significant. Interest in a low diastolic blood pressure has been heightened by information indicating that the wide pulse pressure found in hypertension is also a cardiovascular risk factor (33–35). This is true even among normotensive patients with left ventricular dysfunction after myocardial infarction (36), those with left ventricular dysfunc-

tion (37), and those in the Framingham Study population (38). In the Framingham Study, pulse pressure was the best predictor of cardiovascular risk, but at any given systolic pressure, an inverse relation was noted between diastolic pressure and coronary heart disease incidents. Although a wide pulse pressure is due less to a low diastolic blood pressure than to a high systolic blood pressure (39), the combination of the two, for reasons outlined here, could be the biggest risk factor in isolated systolic hypertension—the high systolic blood pressure increases the demand for left ventricular work, and the reduced mean diastolic pressure is a potential risk factor in patients with significant coronary heart disease.

If the J curve, a low diastolic blood pressure, and a wide pulse pressure are significant issues, how can an elevated systolic blood pressure be beneficially reduced in isolated systolic hypertension without adding the suspected risk for diastolic hypotension? Certainly, a normal baseline diastolic pressure in patients with isolated systolic hypertension should not dissuade clinicians from gaining the well-established benefits of prescribing antihypertensive therapy to decrease an elevated systolic blood pressure. Any agent that reduces peripheral resistance without changing the cardiac output will reduce the mean blood pressure and both the systolic and diastolic blood pressure, which oscillate around it.

Reduction of the mean blood pressure will improve aortic distensibility and narrow the pulse pressure by decreasing the systolic pressure more than the diastolic blood pressure. However, an ideal therapeutic agent in isolated systolic hypertension would have a direct relaxing effect on a stiffened aorta or the peripheral conduit arterial tree. Such an agent would decrease the systolic blood pressure and possibly increase the mean and even the minimum diastolic blood pressure by reversing the mechanisms described. Calcium-channel antagonists have such an action, as do angiotensin-converting enzyme inhibitors, but nitrates are among the best agents for relaxing the conduit arteries (40). If nitrates are effective in patients with isolated systolic hypertension, their mild effect on resistance vessels and peripheral veins would reduce the mean blood pressure, but if they increased arterial distensibility and changed the timing of reflected waves, systolic blood pressure should decrease and diastolic blood pressure should decrease less or increase—an ideal combination in these patients. Such changes would be best measured as surrogates of aortic pressure (by using carotid artery applanation or radial artery transfer functions), and if these changes are found, clinical studies of the effect of nitrates and other agents on aortic distensibility in small patient groups could be done. Although these ideas are attractive in theory, little clinical evidence suggests that minimizing the reduction in diastolic pressure or even allowing it to increase during antihypertensive therapy is beneficial.

In summary, normal or low diastolic pressure is the defining characteristic that makes isolated systolic hypertension clinically different from essential hypertension. Understanding why the diastolic pressure is not also elevated requires some understanding of aortic distensibility and its loss with aging. Through several described mechanisms, increased aortic stiffness increases the systolic pressure but keeps the diastolic pressure normal or even a bit lower. The accuracy of cuff diastolic pressure is also a problem. In elderly persons and patients with isolated systolic hypertension, cuff systolic pressures fairly well represent intra-arterial brachial pressure and intra-aortic pressure. However, cuff-measured diastolic pressures systematically overestimate the intra-arterial brachial artery pressure. Whether the cuff or intra-arterial brachial artery pressure best represents the aortic diastolic pressure in patients with isolated systolic hypertension is not known. The problem of diastolic blood pressure measurement may explain some of the controversy surrounding the J curve.

When cuff pressures are used, the best risk predictor at present seems to be elevated systolic pressure plus a normal or low diastolic pressure: that is, a wide pulse pressure. However, at every given systolic pressure, a lower diastolic pressure carries greater cardiovascular risk, and the problem of a therapeutically reduced diastolic pressure, especially in patients with coronary heart disease, persists. Routine catheter measurements of aortic diastolic pressure in adequate numbers of patients with isolated systolic hypertension is impractical, but a calculated aortic pressure from applanated carotid or radial pulses may supply some answers. In the meantime, the elevated systolic pressure in isolated systolic hypertension requires therapy, but large reductions in cuff diastolic pressures, especially in patients with known coronary heart disease, should probably be avoided.

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