Isolated Systolic Hypertension in the Elderly

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Isolated systolic hypertension (ISH) is a common disorder in the elderly. Several studies have shown a constant positive and graded association between the level of systolic blood pressure and subsequent mortality from cardiovascular disease and stroke. ISH is defined as an elevated systolic pressure above 160mmHg and a diastolic pressure below 90mmHg. Arterial stiffening is the main cause of increasing systolic pressure in the elderly. The finding of high systolic blood pressure with diastolic below 90mmHg is a marker of higher cardiovascular risk and an indication to follow this patient more closely. The placebo-controlled SHEP and Syst-Eur trials have demonstrated that the treatment of ISH with diuretics or long-acting calcium channel blockers results in a marked reduction in cardiovascular events and stroke.

Key words: hypertension, isolated systolic hypertension, clinical trials, drug therapy, elderly.

Introduction
Hypertension is an established risk factor for cardiovascular disease morbidity and mortality. Results of prospective epidemiological studies in different population groups indicate a constant positive and graded association between the level of systolic blood pressure and subsequent mortality from cardiovascular disease and stroke—especially with advancing age—irrespective of the level of diastolic blood pressure.

Definition
Isolated systolic hypertension (ISH) is defined as an elevated systolic pressure above 160mmHg and a diastolic pressure that is below 90mmHg (Table 1).1 The MRFIT study demonstrated that as well as a graded, increased risk with higher systolic blood pressure, there was a particularly high risk for those with the highest systolic blood pressure and the lowest diastolic blood pressure.2 This was recently confirmed by a prospective study of over 9,000 people with hypertension 65 years and older followed for an average of 10.6 years.3

Incidence
This disorder is primarily seen in older patients. Data from the Framingham Heart Study have shown that the systolic pressure rises and the diastolic pressure falls after the age of 60 years in both the normotensive and untreated hypertensive subjects (Figure 1).4 ISH rises in prevalence from 8% in individuals aged 70 and older to 25% in those 80 and older.5 The elevation in pulse pressure in this setting is primarily due to diminished arterial compliance. In the group 50 years and older with either untreated or inadequately treated hypertension, 80% have isolated systolic hypertension.6

Importance
ISH is associated with a two- to four-fold increase in the risk of myocardial infarction, left ventricular hypertrophy, stroke and cardiovascular mortality.7 The peak systolic pressure promotes the development of heart failure and atherosclerosis by increasing cardiac work and predisposing to vascular endothelial injury.

Pathogenesis
One factor which may play a pivotal role in the pathogenesis of ISH is age-related aortic stiffening.8 The ascending and descending aorta dilate with age, with the aortic diameter increasing by 15–35% from age 20–80. Histological changes occurring with normal aging include distorted normal orientation of the laminar unit, fracturing and fragmentation of the elastin fibres and increased collagen content of the vessel wall. These changes influence the aortic pulse, systemic pressure and ventricular performance.

In addition, age-related changes occur in the arterial pulse. Left ventricular ejection creates a pressure wave that travels the length of the aorta to the periphery at a faster rate than blood flow. The velocity of the pressure wave is termed the pulse wave velocity.9 The pulse wave velocity is measured by recording the pulse wave at two sites, usually the carotid and femoral arteries. It is calculated as the distance from the carotid to the femoral artery divided by the time required for the pulse wave to travel this distance. With normal aging, the speed with which the pulse moves along the aorta markedly increases (Figure 2). In older subjects, the faster pulse wave velocity and wave reflection result in the reflected wave traveling back to the heart to reach the ascending aorta in late systole rather than early diastole. This causes an elevation in the systolic blood pressure and a fall in the diastolic blood pressure (wider pulse pressure). Normally, the reflected wave arriving back in early diastole results in

### Table 1

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<th>Classification of Hypertension According to WHO/ISH</th>
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<td>Category</td>
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<tr>
<td>Isolated systolic hypertension</td>
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<td>Subgroup: borderline</td>
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pressure for coronary perfusion much like the effect of intra-aortic balloon counterpulsation, and its loss due to increased arterial stiffness will lead to reduced diastolic coronary perfusion and increased systolic work. Therefore, age-related aortic stiffening contributes to the prevalence of isolated systolic hypertension in the elderly and to a greater risk of cardiac ischemia.

Age-related changes leading to ISH have important physiologic associations. In multiple studies, the systolic blood pressure and pulse pressure are stronger risk factors for cardiovascular disease in older subjects than the mean arterial pressure or the diastolic pressure. Treatment that lowers blood pressure in patients with isolated systolic hypertension is associated with significant reduction in cardiac and cerebrovascular events.

**Treatment**

The SHEP (Systolic Hypertension in the Elderly) trial was the first to demonstrate that people with ISH could not only benefit from therapy, but were also a much higher risk group than previously thought. Although 15 years later it is hard to believe that it used to be ethically to treat elderly ISH patients with a placebo, the state of knowledge at the time was such that this was reasonable. In this study, 4,736 patients with ISH were randomized to either active antihypertensive therapy with diuretics or placebo, with the aim to reduce systolic blood pressure by at least 20 mmHg or to a level below 160 mmHg. Achieved blood pressures were 143/68 mmHg in the treatment group compared to 155/72 mmHg in the placebo arm. At four to five years, the incidence of stroke was reduced from 8.2% in the placebo group to 5.2% in the treated group (a 36% relative risk reduction and a 3% absolute risk reduction, with a number needed to treat of only 33 for the outcome stroke). A similar reduction was noted in cardiac events as well. The Syst-Eur trial, which randomized 4,695 patients with ISH to placebo or nitrendipine—a dihydropyridine calcium channel blocker—also demonstrated a risk reduction equivalent to that found in the SHEP trial for both stroke and cardiovascular mortality.

One issue that is frequently raised in the treatment of ISH is what happens if the diastolic blood pressure falls too low. However, we know from placebo-controlled trials such as SHEP and Syst-Eur that treatment of these patients is better than no treatment at all. In a meta-analysis of clinical trials with a total of 15,693 people with ISH, active treatment reduced total mortality by 13%, all stroke by 30% and all coronary events by 23%.

**Choice of Therapy**

Based on the results of the SHEP and Syst-Eur trials, low-dose thiazide therapy is the preferred initial therapy for ISH. Hydrochlorothiazide at 12.5 or 25 mg has the advantage of low cost, efficacy and proven benefit. The Syst-Eur trial demonstrated the safety and efficacy of long-acting dihydropyridine calcium antagonists for the treatment of ISH (Figure 3).

It is recommended that all people older than 65 years have their blood pressure taken at least annually if they are normotensive, and every three to six months if their high blood pressure has been controlled. The finding of high systolic blood pressure with diastolic below 90 mmHg is a marker of higher cardiovascular risk, and this patient must be followed more closely. Recently ambulatory blood pressure monitoring has been found to be a better predictor of adverse outcomes in older patients with widened pulse pressure and ISH. Home monitoring with an approved device may be a better way to monitor therapy and eliminate a white coat effect.

**Prevention**

Prevention of age-related aortic changes is possible with both lifestyle changes and drug therapy. Modifying lifestyle factors to lower blood pressure—such as weight loss, regular aerobic exercise, diet with low sodium content, cessation of smoking, moderation of alcohol intake and management of dyslipidemia and blood sugar control—will help to protect the vascular tree.

**Future**

The clinical utility of measuring parameters of arterial stiffness beyond the pulse pressure have not yet been determined. However, in the future serial
Isolated Systolic Hypertension

Increased systolic pressure

Left ventricular ejection creates pressure wave through aorta to periphery

Pressure wave reflected back in early diastole

To counteract reflected pressure wave, cardiac muscle must contract harder in systole, thereby increasing systolic blood pressure

Faster pulse wave velocity causes reflected wave to travel back to heart in late systole rather than early diastole

Figure 2: The Pathogenesis of Isolated Systolic Hypertension
measurements of arterial tonometry and pulse wave velocity to assess the effects of therapeutic interventions will provide more specific, clinically important information unavailable from the measurement of blood pressure alone. The focus of ISH treatment is to bring down the systolic blood pressure. In the future, ISH may no longer remain a separate entity in clinical practice guidelines, as treatment of high blood pressure will be initiated if blood pressure in the uncomplicated patient is greater than 140 systolic and/or 90 diastolic. Therefore, having a separate category for those with systolic pressure greater than 160 and diastolic less than 90 will be redundant. Today, however, there are a large number of treatment trials involving patients with ISH that help guide treatment in this higher risk group of hypertensives.

**Conclusion**

In summary, ISH is associated with a higher risk of cardiovascular disease and mortality. Wider pulse pressure in ISH is a marker of loss of vascular elasticity associated with hardening of the arteries. Treatment of ISH has been proven to be beneficial. The goal should be to bring the systolic blood pressure down to 140mmHg, or at least by 20mmHg. Multiple medications may be required. Because patients with ISH are at high risk, they should be assessed for multiple cardiovascular risk reduction strategies.

**No competing financial interests declared.**

**References**