



HEALTHY HEART

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Systolic Blood Pressure (SBP) rises progressively with age, while after about the age of 65 there is a modest decline. Isolated Systolic Hypertension (ISH) with increased pulse pressure (Figure 1) is the commonest form of hypertension in the elderly and is a major risk factor for cardiovascular (CV) disease. ISH is defined as SBP >140 mmHg and Diastolic Blood Pressure (DBP) <90 mmHg. It should probably be distinguished from essential hypertension (where SBP and DBP are both increased). Pathogenesis of the two conditions overlaps, but is not identical. There are subtle differences in the approach to treatment. ISH and essential hypertension are not entirely distinct – a patient with essential hypertension may later present with ISH as the DBP decreases with age. However, over 60% of patients with ISH have no preceding hypertension. ISH affects two-thirds of patients over 65 years and three-quarters of patients over 75. It is by far the most common form of hypertension in later life (Figure 2). With the ageing population, this is clearly a very major public health problem.

Isolated Systolic Hypertension

Case History

A 75-year-old man who is a care taker for his disabled wife.

He is quite active and copes well with household chores. He has high cholesterol and takes a statin as well as aspirin. Blood pressure (BP) has been high for some time, and at the visit is 168/82. The time has come to start treatment, and you wish to discuss this with him. Renal function and creatinine are both normal. Urine is negative on stick testing but he has microalbuminuria on laboratory testing.

- Is ISH common, and is it important?
- Why does Systolic BP (SBP) selectively increase in the elderly?
- What is the optimal approach to management?

The relative increase in SBP, compared with DBP, relates to decreased vascular compliance with ageing. The latter arises from atherosclerosis, collagen cross-linking and glycosylation, vascular calcification and elastin fragmentation. The aorta and larger

vessels lose the ability to expand to accommodate the pulse wave during systole and there is decreased recoil during diastole. Decreased baroreceptor responses and increased salt sensitivity contribute to hypertension in the elderly. Although plasma catecholamines are relatively increased, sensitivity of adrenoreceptors is decreased. Increased

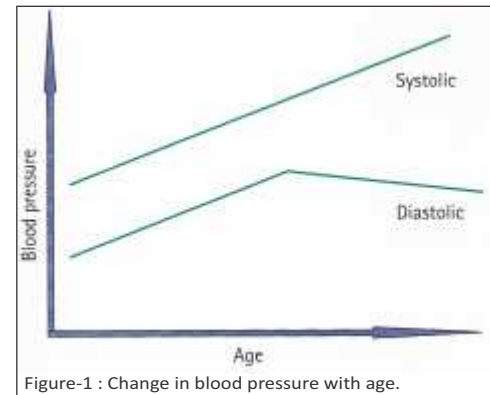


Figure-1 : Change in blood pressure with age.

sympathetic drive is, therefore, a less important mechanism and because of this as well as often decreased myocardial function, increased cardiac output is less important than in younger subjects. Activation of the

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renal artery stenosis is also relatively less important in ISH, explaining why angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are often not the most effective drugs. The addition of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers to treatment is logical where ISH is placing the patient in

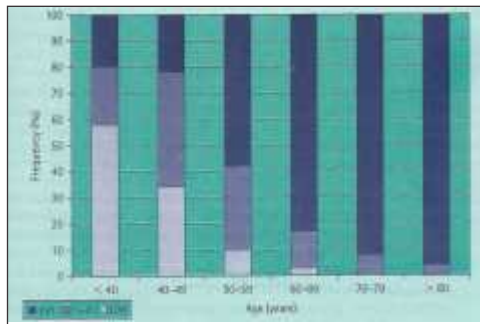


Figure-2 : Presentation of untreated hypertension. IDH, isolated diastolic hypertension; ISH, isolated systolic hypertension; S-D, systolic-diastolic (essential) hypertension. Adapted from Chobanian.

danger of end-organ damage. There is particularly strong evidence that these agents may bring about regression of left ventricular hypertrophy and retard the development of nephropathy. Salt sensitivity is increased in older subjects, and this contributes to increased arterial stiffness. Thus, lower salt intake and diuretic therapy are central in management. ISH and essential hypertension are compared in Table 1.

Even a modest decrease in SBP of <5 mmHg reduces cardiac mortality by 7%

Table-1 : ISH and essential hypertension

	Essential	ISH
Increase cardiac output	+	-
Arterial compliance	+	-
Peripheral resistance	++	+
Left ventricular mass	+	++
Baroreceptor sensitivity	--	-
Plasma catecholamines	+	++
Plasma renin	-	-
Salt sensitivity	+	++

Adapted from Pannarale.

and stroke mortality by 10%. A target BP of 140/90 seems reasonable for the elderly, but is often not achievable, let alone the tighter target of 130/80, which is recommended for those at higher risk (e.g. those with diabetes and chronic kidney disease). Effective treatment of ISH decreases the risk of CV events by 23%. The landmark trials in this area (see Duprez for a review) were:

- SHEP (1991) followed 4736 patients with ISH for 4.5 years. In treated patients, the rate of non-fatal stroke was decreased by 36%, cardiac disease by 25%, and heart failure by 53%. A more recent (2005) extension of this study following patients for up to 14.3 years showed continuing benefit in terms of event rate reduction. Benefit extended to those with pre-existing diabetes, while those who

developed diabetes during the follow-up period but had their BP treated had no different risk to patients without diabetes. This study was based on the use of chlorthalidone with other agents added as needed.

- Syst-Eur (1997) and Syst-China (1998) followed 4695 and 2394 patients respectively for 2-3 years, with initial therapy based on Calcium Channel Blockers (CCB). These studies showed a reduction in stroke of about 40% and of total CV outcomes of 31-39% for treated patients.

More recent studies have included: LIFE (2002) in which losartan decreased CV out-comes compared with an atenolol-based regimen in 1326 patients with ISH and left



ventricular hypertrophy followed for 4.7 years; the Systolic Hypertension in the Elderly Long-term Lacidipine study (SHELL, 2003) in which 1882 patients with ISH were followed for 32 months, showed a 9.3% reduction in event rate with the CCB; the Intervention as a Goal in Hypertension Treatment study (INSIGHT, 2004) which included 1498 patients with ISH followed for 3 years, and showed a 6% decrease in the CV event rate. These, and a number of other short-term studies have, in recent years, highlighted ISH as a clinical problem in the elderly. They have also shown that decreasing BP leads to lower CV risk. Although the various classes of agent are similar in BP-decreasing potency, rennin-angiotensin system blocking drugs and CCBs have the most trial evidence. The former may be slightly superior in preventing stroke and are slightly better tolerated because of the relatively high incidence of peripheral oedema seen with CCBs.

Treatment of ISH

As with all patients with hypertension, the elderly with ISH should have an overall assessment of CV risk, secondary causes of hypertension should be considered (particularly renovascular) and they should be screened for end-organ damage (eyes, heart and kidneys). Consider also conditions that increase cardiac output and may selectively increase SBP. These include anaemia,

thyrotoxicosis, Paget's disease and aortic regurgitation. Lifestyle modifications should be instituted where possible – maintain or decrease body weight, regular exercise, balanced diet, lower salt intake and avoid excess alcohol. It is assumed that the major advantage of drug treatment is through lowering BP, and none of the major classes has a specific action in ISH. In the elderly, it is important to start with low doses of drugs where possible, and to titrate gradually with careful monitoring of BP response, renal function and electrolytes. Over-vigorous reduction in DBP should be avoided as this may decrease myocardial perfusion.

The first choice of treatment for ISH is low-dose thiazide. The greatest evidence is with hydrochlorothiazide and chlorthalidone. Bendrofluazide is also widely used. The latter is more potent on a milligram for milligram basis and also has a longer half-life (48-72h vs 16-24 h). The disadvantages of thiazides are hypokalemia, increased uric acid, dyslipidaemia, hyperglycaemia, and erectile dysfunction in men. All of these are common in the elderly but less likely to occur with low doses – 12.5 mg of hydrochlorothiazide is a suitable starting dose. Long-acting CCBs should also be considered early in the treatment. These are of proven efficacy and have beneficial effects on vascular remodelling. B-blockers are no longer considered first-line for the elderly patient with ISH, but should

certainly be used in those with angina or previous myocardial infarction, and considered in those with heart failure (Figure 3).

Recent Developments

1. High SBP is very variable in older subjects with reduced vascular compliance. There is an argument for confirming ISH on at least three occasions before the diagnostic label is assigned. A recent large Portuguese study confirmed that ISH was common, particularly after the age of 70. It was not, however, particularly associated with premature mortality, and CV complications often developed very late in life.
2. In a follow-up of participants in the SHEP trial at 14.3 years, a chlorthalidone-based antihypertensive regimen decreased CV mortality – RR 0.86 (95% CI:0.76 to 0.98). Patients who had sustained stroke experienced a particularly poor mortality experience. We should not be over-pessimistic about the dangers of ISH, or over-optimistic about the benefits of treatment. For population-based risk reduction, many patients would have to be treated for many years to appreciably impact on mortality.
3. Over-aggressive treatment of systolic hypertension may lead to an unwanted decrease in DBP. In the elderly, DBP <60 mmHg has been associated with poor



prognosis independent of large artery stiffness and left ventricular function. Elderly people taking antihypertensives should be carefully monitored. DBP decreases with age and may warrant altering treatment for ISH.

4. Long-acting CCBs are a very useful adjunct to thiazides as first-line treatment. A recent trial compared amlodipine with a newer CCB manidipine. Chlorthalidone was added where needed. Both CCBs effectively decreased BP. Manidipine had the advantage of a lower incidence of peripheral oedema.
5. The importance of exercise as an intervention for the elderly is often forgotten. Apart from general well-being, exercise has tangible benefits including reducing SBP. Given the now proven benefits of exercise in elderly patients with chronic disease, including diabetes and pulmonary disease, we need to examine how to actively engage elderly people in exercise programmes.

younger subjects to more mechanical causes in the elderly. This explains why some drugs are less effective in ISH. The condition is important, being strongly linked with adverse CV outcomes, particularly stroke. Treatment with two or more drugs is often needed. Over-vigorous

treatment may control ISH but at the expense of undue lowering of DBP, which may reduce coronary perfusion. Low-dose thiazides and long-acting CCBs are the cornerstone of treatment. These should be initiated cautiously and titrated gradually, especially in very aged or frail patients.

Conclusions

The vast majority of us will develop hypertension as we age, and ISH is by far the commonest form in older people. Subtly, the pathogenesis is different to that of essential hypertension, which is a disease of younger people. Decreased vascular compliance is the hallmark. The underlying cause of hypertension shifts from more humoral mechanisms in

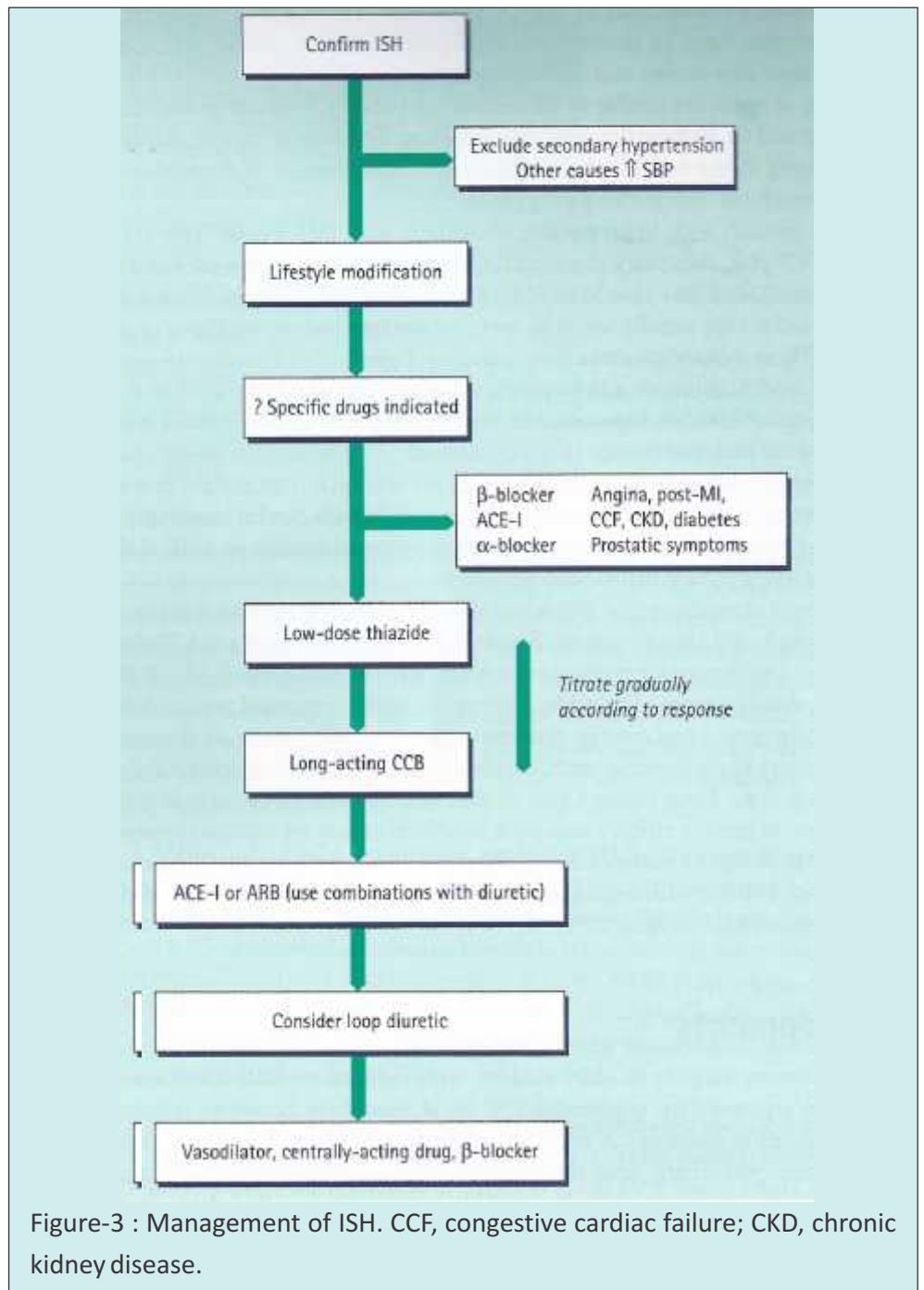
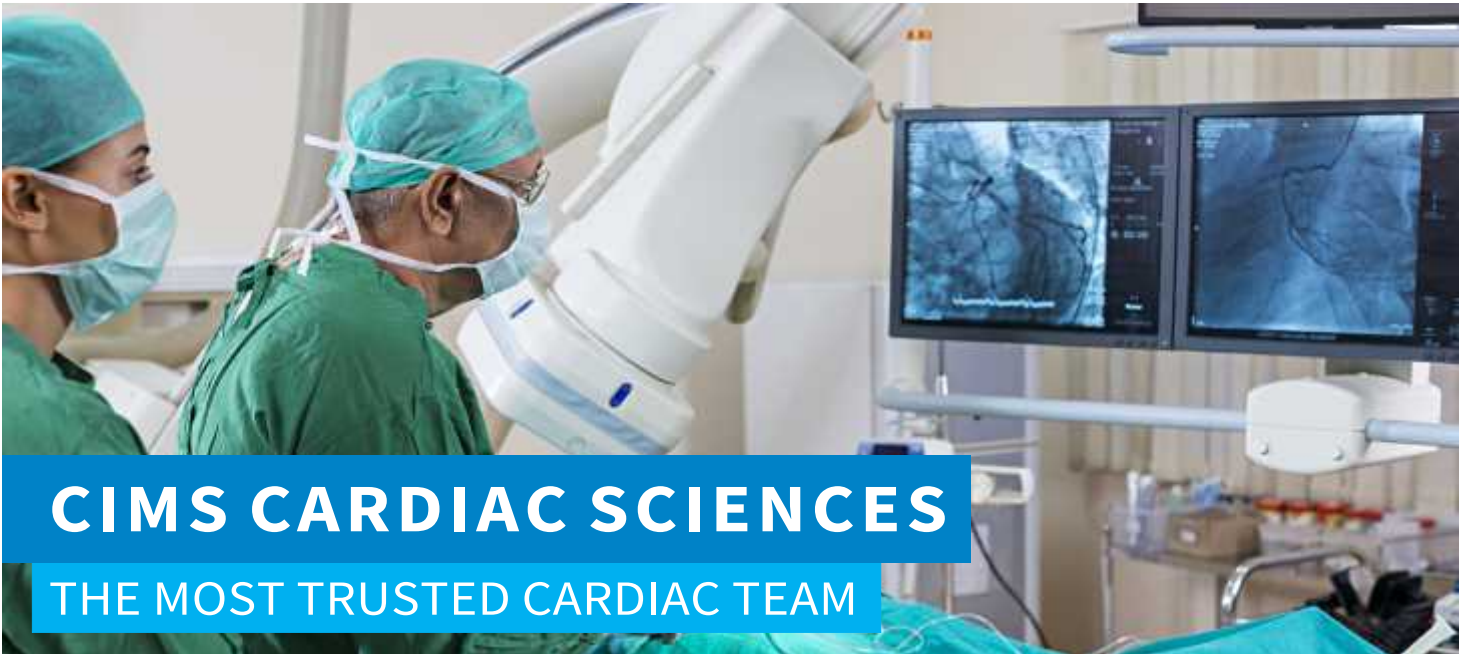


Figure-3 : Management of ISH. CCF, congestive cardiac failure; CKD, chronic kidney disease.



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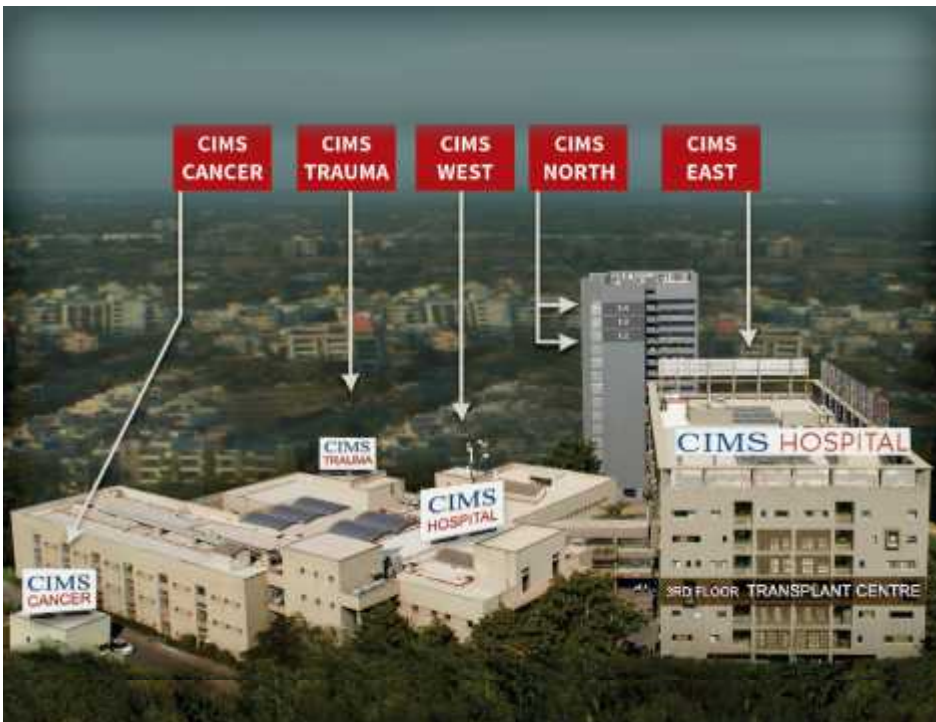
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