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Hot topics in the management of hypertension

A report from the Big Picture Meeting, Stellenbosch, March 2020

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Introduction

As a continent, Africa faces a huge burden of morbidity and mortality from hypertension, as diagnosed internationally at the cut-off of >140/90mmHg. In South Africa, 42% of deaths in adults over the age of 30 years are attributable to hypertension, which outstrips total deaths from ischaemic heart disease. Blood pressure (BP) control is the most cost-effective method of reducing cardiovascular events; a drop of 10mmHg will reduce deaths across the entire vascular continuum: ischaemic events by 20%, coronary heart disease by 20% and strokes by 27%.[1]

Despite the existence of effective medications, BP is seldom adequately controlled. Only 50% of patients with raised BP are ever diagnosed as hypertensive and of those diagnosed and treated, only one in three reach their target BP levels. This review will focus on the presentation at the Big Picture meeting, which dealt with the more challenging aspects of BP management. "As clinicians, we need to do better," Dr Nash Ranjith, Nelson R Mandela School of Medicine, Durban, noted.

Isolated systolic hypertension in the old and young

"As clinicians, we need to do better with regard to blood pressure management"
Dr Nash Ranjith

KEY CLINICAL MESSAGES

- ✓ Isolated systolic hypertension (ISH) in the elderly (80 years and older) results in an increased risk of mortality
- ✓ White coat hypertension is very significant in this elderly cohort and the presence of ISH must be determined using out-of-office BP measurement, preferably ambulatory BP measurement (ABPM), to assess the degree of systolic hypertension
- ✓ Most experts agree that medication should seek to lower systolic BP; while diastolic BP is inevitably also lowered, it should be to the level that the individual elderly patient can tolerate. This point of view is, however, still open to controversy/debate.

ISH in the elderly

A clinical scenario commonly encountered in general practice is that of the elderly patient, likely to have been on BP-lowering medication, who now presents with a very raised systolic BP (>150mmHg), a reduced diastolic BP and a resultant wide pulse pressure that signifies a very high risk for a vascular event. The reason for the increase in systolic BP in the older patient is arterial stiffness, which leads to a rapid reflected wave that augments the systolic BP.

The absolute risk of stroke mortality in terms of usual systolic BP was evaluated by the Prospective Studies Collaboration in a meta-analysis of 61 studies involving more than one million adults (Figure 1).[2] The annual absolute difference in stroke risk is

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greater in old age. Confirmation of these data was obtained in the HYVET randomised double-blind trial of patients aged 80 years or older, where treatment of ISH with indapamide and perindopril reduced strokes by 30%, total mortality by 21% and heart failure by 64%[3] – a remarkable reduction in mortality in the super-elderly treated for ISH. Also, in the SPRINT trial of patients over the age of 75 years, BP treatment significantly reduced the rates of fatal and non-fatal major cardiovascular events and death from any cause.[4]

Guidelines on treating ISH differ: the European Society of Cardiology/European Society of Hypertension (ESC/ESH) 2018 guidelines propose a systolic BP <140mmHg in over 80-year-olds if this is tolerated, but antihypertensive therapy should aim to keep diastolic BP at a level of 70-80mmHg.[5] On the other hand, the American College of Cardiology/American Heart Association (ACC/AHA) 2017 guidelines are less prescriptive with regard to treatment targets for all adults, and propose a target of <140/80mmHg.[6] Observational studies such as the SYST-EUR study have, however, pointed to a mortality increase if diastolic BP is reduced below 60mmHg.[7]

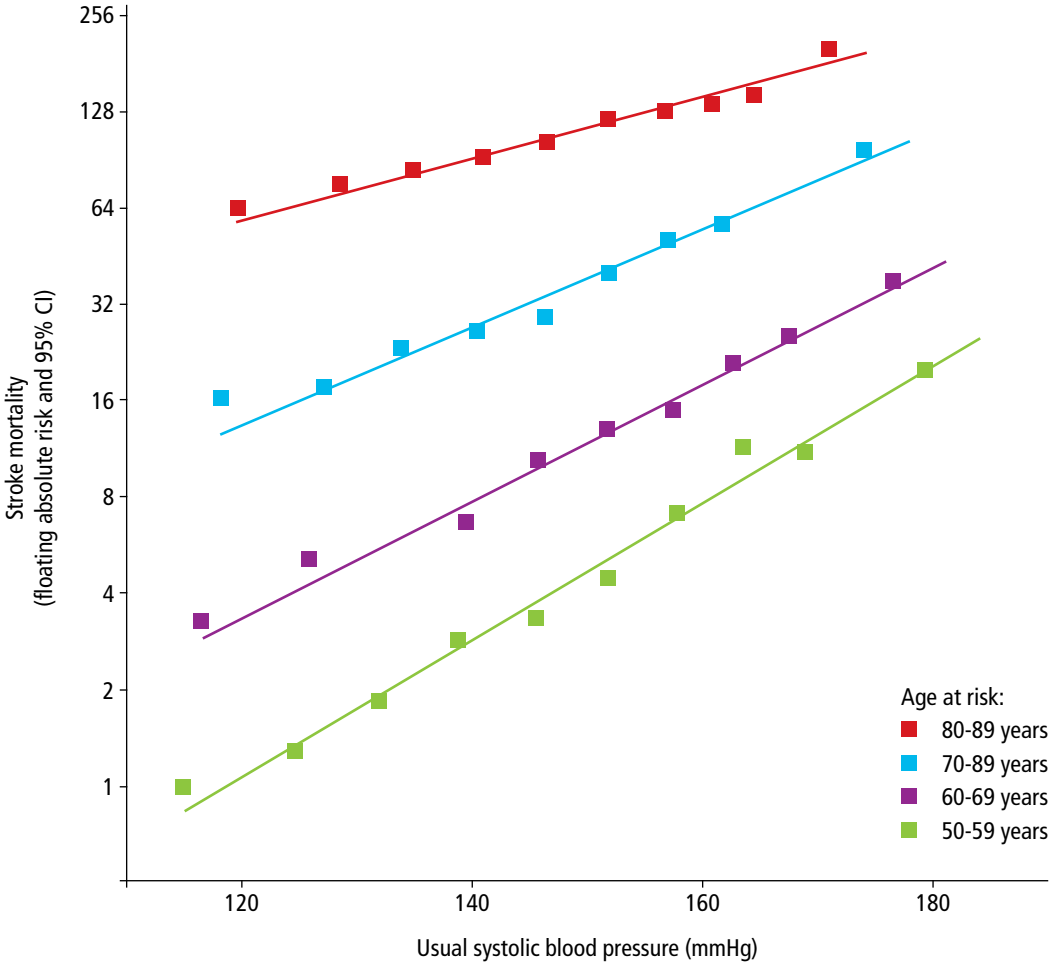

Figure 1. Ageing and cardiovascular risk

Role of white coat hypertension in the elderly with ISH

Very importantly, when you make a clinical decision about treating ISH in the elderly, you need to consider the confounding factor of white coat hypertension. In the HYVET study, a smaller group within the cohort were evaluated using in-office or out-of-office ABPM (Table 1). The difference in measurement of systolic BP was in excess of 30mmHg, with in-office measurements being much higher. "It is vital that clinicians use out-of-office BP measurement when assessing the presence of ISH," Professor Rayner stressed.

Table 1. HYVET study clinic BP and ambulatory BP at baseline: mean (SD) and range		
Blood pressure	**Mean (SD)**	**Range**
Systolic		
CBP sitting	172 (8)	159–197
CBP standing	168 (10)	149–197
Baseline morning ABP (8:00 AM–12:00 noon)	140 (20)	101–201
Baseline daytime ABP (8:00 AM–8:00 PM)	136 (16)	105–174
Baseline night-time ABP (10:00 PM–6:00 AM)	124 (20)	90–217
Baseline 24h ABP	133 (15)	104–187
Difference between CBP sitting and ABP morning	32 (21)	–33 to 80
Difference between CBP sitting and ABP daytime	36 (16)	–13 to 73

Is there a J-curve point in diastolic BP that leads to non-treatment of ISH in the elderly?

"It is vital that you use out-of-office BP measurement when assessing ISH"
Professor Rayner

This question was investigated in one million patients in a study that related systolic and diastolic BP reduction to cardiovascular outcomes.[8] While a J-curve relationship between diastolic BP and outcomes was seen, this was explained at least in part by corrections for age and other covariates and by a higher effect of systolic hypertension among persons in the lowest quartile of diastolic BP. The view of Professor Rayner is: "In suspected ISH, the first step is to undertake 24-hour ABPM. If ISH is present, treatment should be instituted. Aim for a systolic BP <140 mmHg: provided this is tolerated, ignore the diastolic pressure."

ISH in the young patient

Firstly, it is important to point out that there are very few data on the value of treating BP in the young and no randomised clinical trials have ever been done in the age group <25 years. Hypertension in young people is an important topic in South Africa, as the first decade of this millennium saw a doubling of the prevalence rate among adolescents and young adults aged 15-24 years.[9] The majority of young patients will have primary hypertension, while about 10% will have secondary hypertension (Table 2).[10]

Table 2. Causes of secondary hypertension in the young
• Renal parenchymal disease, e.g. glomerulonephritis
• Renovascular disease, e.g. renal artery stenosis
• Mineralocorticoid-mediated hypertension, e.g. primary hyperaldosteronism
• Catecholamine-mediated hypertension, e.g. phaeochromocytomas
• Medication, e.g. the oral contraceptive pill
• Abuse of cocaine or amphetamines
• Coarctation of the aorta
• Rarer causes

A treatment approach for primary hypertension in the young has recently been proposed and includes the steps outlined in Table 3.[10]

Table 3. An approach to the treatment of primary hypertension in the young (<30 years)[10]
• Lifestyle changes (weight loss, diet and exercise)
• Assessment of lifetime cardiovascular risk or heart age
• Joint decision-making and a personalised approach
• Consideration of drug treatment if BP >140/90mmHg or there is evidence of organ damage or increased cardiovascular risk due to comorbidities. Consider using:
– An angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker or beta-blocker
– A calcium channel blocker if the patient is a black African or of Afro-Caribbean origin, or if there is a possibility of pregnancy.

However, the issue of ISH in the young is very controversial and it may not represent a true hypertensive state. Studies have shown that the amplification of the pulse wave from the aorta to the brachial artery may be spuriously elevated in young people, leading to an incorrect diagnosis of hypertension and inappropriate antihypertensive therapy. This is not solved by 24-hour ABPM or home BP monitoring, as the same phenomenon remains present.

In the absence of overt hypertensive organ damage, it is essential to perform pulse wave analysis to determine the central aortic pressure, pulse wave velocity and augmentation index. This can only be performed in specialised centres. In patients with 'spurious ISH', these indices are normal and the patient can be reassured. However, long-term follow-up is required.

Chronotherapy: When to give antihypertensives?

It is important to realise that while office BP measurement is a potent indicator of risk of future cardiovascular events, night-time BP is the most powerful indicator of cardiovascular death

It is important to realise that while office BP measurement is a potent indicator of risk of future cardiovascular events, night-time BP is the most powerful indicator of cardiovascular death. "As the use of ABPM increases in daily clinical practice we are not only learning more about white coat hypertension and masked hypertension," Professor Rayner reminds us, "but also the important contribution of non-dipping to increased cardiovascular risk and the association between early morning BP surges and cardiovascular events."

Non-dipping is frequently seen when there is chronic kidney disease, and among black African, diabetic and HIV-infected patients. In these patients, it is advantageous to give 24-hour-acting drugs or those requiring twice-daily dosing, or nocturnal dosing of shorter-acting drugs such as losartan, enalapril and cardugen.

The value of night-time dosing of whichever antihypertensive is being used has been shown in a number of studies to be more effective, including in patients with hypertension and diabetes, as evidenced by BP control data obtained from ABPM. In addition, there is a significant 12% cardiovascular risk reduction for each 5mmHg decrease in asleep-systolic BP.

A large study of night-time dosing in about 22 000 patients[11] has recently been published. Unfortunately, while it showed positive results, it was not randomised and the antihypertensives used were not true 24-hour agents (ramipril, enalapril and hydrochlorothiazide). Nonetheless, the study showed cardiovascular risk reduction when these drugs were used at night, rather than during the day. "A proper randomised study of the benefits is still needed to fully justify a switch to night-time dosing," according to Professor Rayner. He concludes: "I believe it is vital that we use antihypertensive agents that are truly effective over 24 hours; but if formularies do not allow this, a practical solution could be to consider twice-daily dosing or a combination of day- and night-time dosing." Another phenomenon often present in the elderly with ISH and stiff arteries is extreme dipping, which is associated with a high risk of silent cerebral infarcts (Figure 2). "In fact, brain damage with white matter lesions are frequently present in hypertensive patients; magnetic resonance imaging is extremely useful to pinpoint this damage, but is unfortunately very expensive" (Figure 3).[11] Although guidelines are available for treatment of this condition it is advised that short-acting daytime antihypertensives be considered.

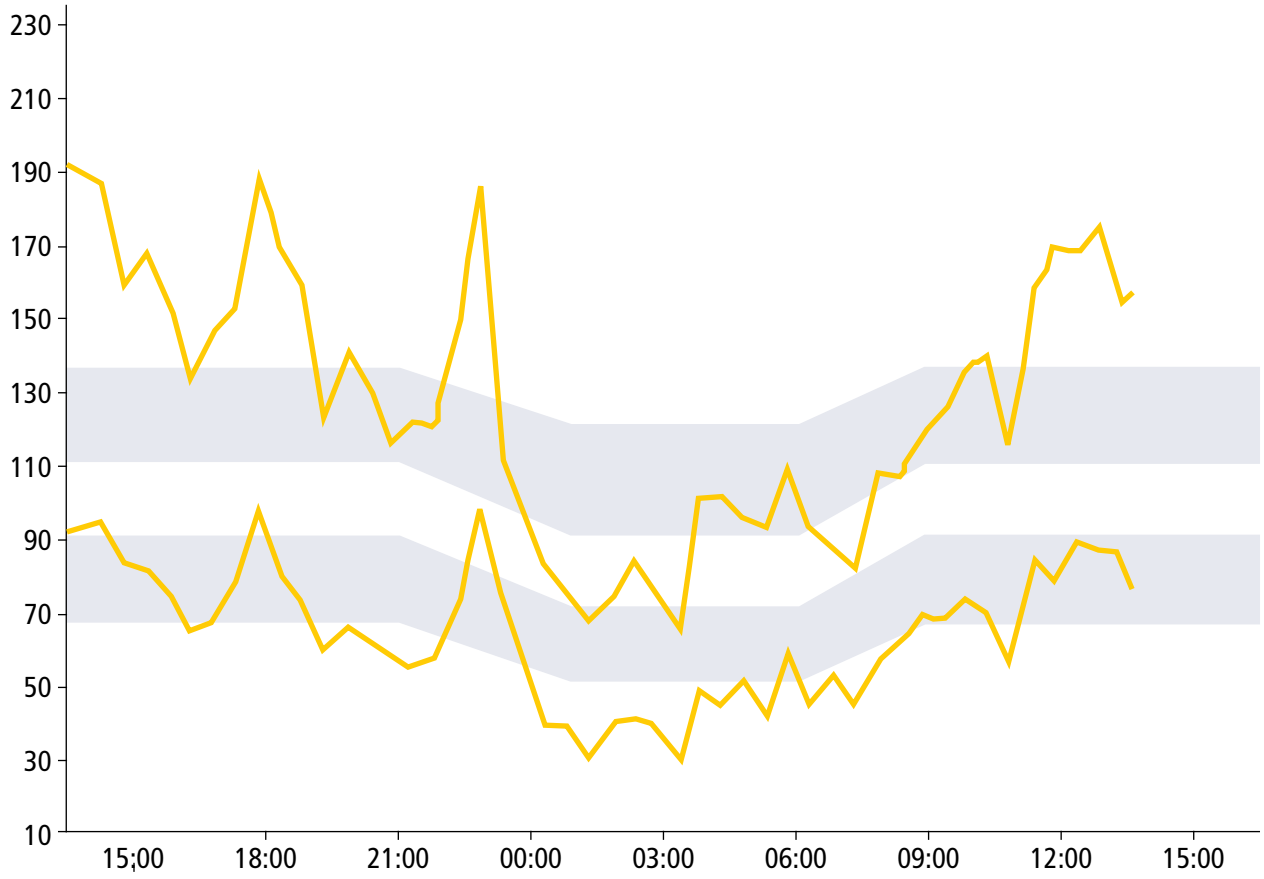

Figure 2. Extreme dipper. Often elderly with ISH and stiff arteries; short-acting morning dose

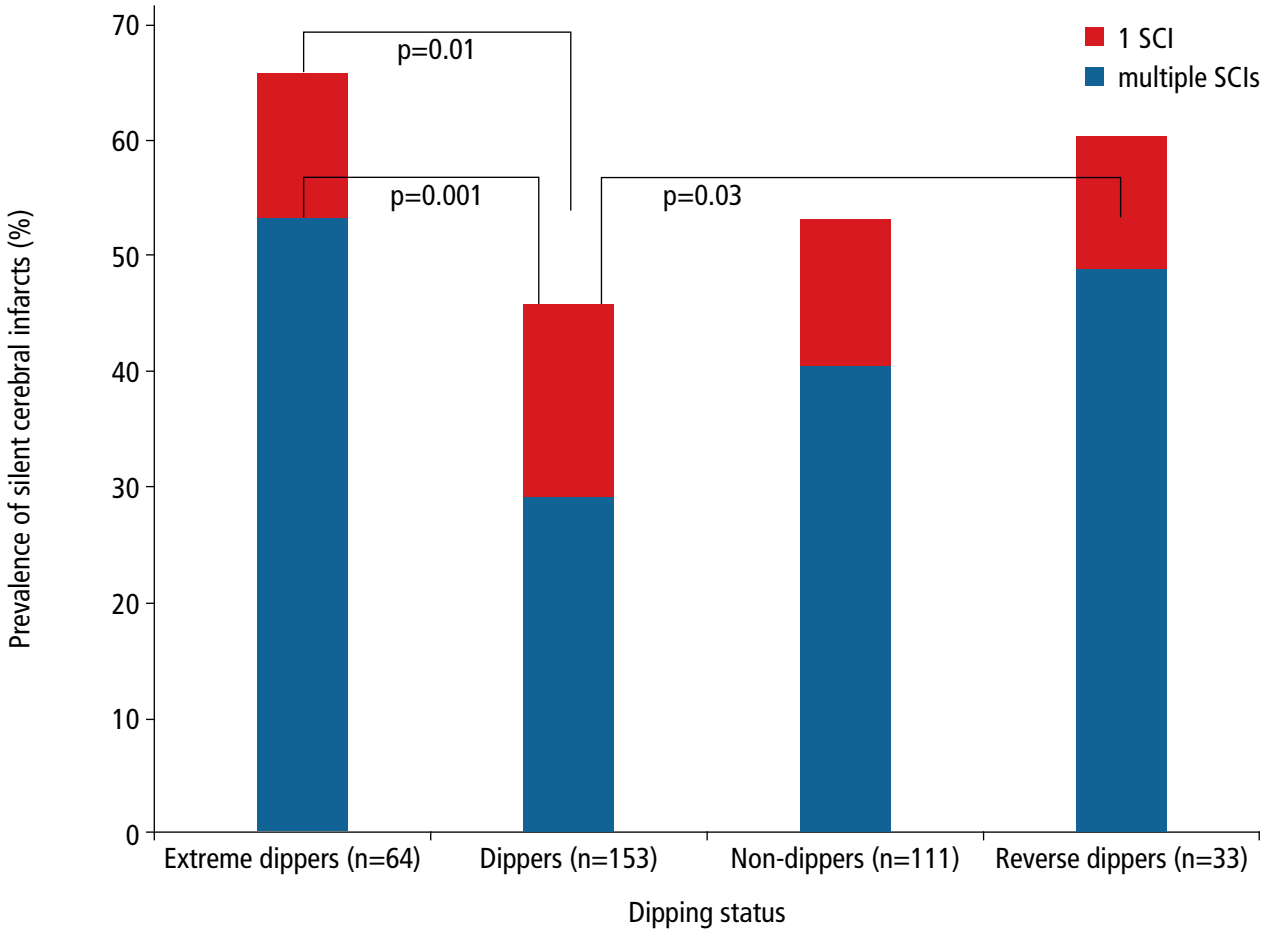

Figure 3. Prevalence of silent cerebral infarcts

KEY LEARNINGS

- A 10mmHg drop in systolic BP will reduce deaths across the entire cardiovascular continuum
- ISH in the elderly signifies a very high risk for a vascular event and treatment substantially reduces adverse events
- Although diastolic BP <60mmHg increases mortality risk, systolic BP should be targeted to <140 mmHg provided this is well tolerated
- Out-of-office ABPM is vital to exclude white coat hypertension
- In South Africa, the prevalence of hypertension is increasing in the young adult population and physicians should be aware that ISH in the young may be spurious
- Night-time non-dipping contributes to increased cardiovascular risk, and night-time antihypertensive treatment may provide benefit. However, physicians should consider 24-hour acting drugs in most circumstances, whether given in the morning or at night.

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