UNIT NO. 2

REDUCTION OF CARDIOVASCULAR RISK THROUGH DETECTION AND TREATMENT OF EPISODIC HYPERTENSION AND BLOOD PRESSURE VARIABILITY

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ABSTRACT

Optimal treatment of hypertension includes both achieving target blood pressure and maintaining normal diurnal variation. Home blood pressure monitoring and ambulatory blood pressure monitoring provide multiple readings in an out-of-office setting and enable the clinician to identify subsets of patients at increased risk despite normal clinic readings. Effective antihypertensive agents are available, especially in combination therapy, to reduce abnormal fluctuations in blood pressure and improve outcome.

Keywords: diurnal variation, home blood pressure monitoring, ambulatory blood pressure monitoring, combination therapy

SFP2011; 37(4) (Supp 1): 10-14

INTRODUCTION

Hypertension is highly prevalent in developed countries and is a major risk factor for cardiovascular and renal diseases. In Singapore, up to 25% of adults aged 30 to 69 years old are reported to be hypertensive by a Ministry of Health survey 1. In a meta-analysis of 61 prospective studies, every increase of 20 mmHg in systolic blood pressure (BP) and 10 mmHg in diastolic BP correlate with doubling of mortality from ischemic heart disease or stroke, and the relationship is similar across all age groups between 40 to 89 years old [2]. Control of BP is an important component of an overall strategy to improve cardiovascular health.

WHAT IS BP VARIABILITY

Hypertension treatment guidelines recommend lowering BP to below target level to reduce end organ damage. Besides achieving the target level of 140/90 mmHg for the general population, it is equally important to assess and control BP variability. In normal circadian rhythm, night-time BP is 10-20% lower than day-time, with a steeper increase in early morning and followed by more gradual increase throughout the awake hours.

This normal circadian rhythm can be disrupted in various subsets of hypertensive patients.

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Some important terminology to note:

- Non-dipper: failure of nocturnal BP to decrease by at least 10% of daytime BP.
- Riser: paradoxical increase of nocturnal BP above the daytime BP.
- Extreme dipper: extremely large night-time BP drop.

ROLE OF BLOOD PRESSURE VARIABILITY IN THE DEVELOPMENT OF CARDIOVASCULAR RISK

Hypertensive patients who exhibit abnormal BP variability have increased risk of end organ damage and poorer outcome. In 2 large hypertension treatment trials, the United Kingdom Transient Ischemia Attack (UK-TIA) and ASCOT-Blood Pressure Lowering Arm (ASCOT-BPLA) trials, excessive variability in systolic BP was associated with increased risk of cardiovascular events [3, 4]. This was postulated to be linked to arterial stiffness, changes in peripheral vascular resistance and structural remodelling of arteries. In particular, the early morning surge in BP is associated with a higher risk of acute myocardial infarction, sudden death and stroke. Hence, cardiovascular risk can remain high in the individual patient whose average BP (usually assessed during clinic visits) falls below target BP but who may still exhibit significant BP variability, especially with an early morning surge. In the ASCOT-BPLA substudy, it was further shown that treatment to reduce BP variability was associated with reduction in cardiovascular event rate.

ROLE OF BLOOD PRESSURE MONITORING IN TRACKING AND CONTROLLING BP VARIABILITY

Clinic BP is the most common method used for detection and monitoring of hypertension. However, it may be fraud with the problem of white coat effect, which may affect as many as up to 20% of patients [5]. On the other hand, some patients with normal BP in the clinic may have pressures that spike to dangerous levels in other situations.

Home BP Monitoring (HBPM) and Ambulatory BP Monitoring (ABPM) eliminate the problem of white coat hypertension but requires greater patient involvement and added costs. They also have the advantage of being able to detect diurnal variation and early morning surge of BP. Both HBPM and ABPM have been shown to provide better prediction of end organ damage and cardiovascular risk compared to clinic BP [6, 7, 8]. These modalities are particularly useful in the elderly who are more prone to BP variability and

white coat effect, as well as patients with diabetes, kidney disease and pregnant women. The advantages of HBPM and ABPM are summarised in Table 1.

The European Society of Hypertension recommends validated, semi-automated devices with self-inflating cuffs for home BP measurement. When done properly, it is a better reflection of BP control compared to isolated clinic BP. Home BP can be taken at trough level of treatment to check on the therapeutic coverage throughout the dose-to-dose time interval. Patients are likely to achieve goals more quickly and be confident that medicines are working for them.

ABPM needs to be performed by a cardiac technician or nurse. It is more costly and less repeatable than HBPM. However, it provides a complete picture of diurnal variation especially the night-time BP profile. The latter has been shown to be superior to day-time ambulatory BP as a predictor of cardiovascular outcome 9. Figures 1 and 2 are examples of a normal and abnormal ABPM tracing respectively.

Table I. Advantages for Ambulatory and Home BP monitoring

Home BP monitoring

- useful for initial diagnosis when suspect white coat effect
- convenient, able to do multiple readings
- easy to perform by self or caregiver
- low-cost monitors are available
- improves adherence and BP control

Ambulatory BP monitoring

- useful for initial diagnosis when suspect white coat effect
- true assessment of diurnal variation
- identifies high risk subgroups (non-dipper, inverse dipping)
- can detect hypotensive episodes especially in elderly and diabetics
- large body of evidence for prognostication

NORMAL VALUES

For Home BP monitoring, 3 readings are recommended, taken 1 minute apart. Although the first reading is typically the highest, an average of the 3 readings is used as the BP reading. The American Society of Hypertension recommends an upper limit of 135/85 mmHg for Home BP [10].

For Ambulatory BP monitoring, the upper limits of normal are 135/85 mmHg for daytime, 120/70 mmHg for night-time and 130/80 mmHg for average BP over 24 hours [5]. As with clinic BP monitoring, a lower goal is advisable for special groups such as diabetes, renal failure and pregnancy.

Choice of Antihypertensive Agents

Effective antihypertensive treatment should lower BP to below target level while maintaining normal 24-hour BP variability. In particular, BP control should prevent the high risk early morning spike when most cardiovascular and cerebrovascular events occur.

Recent data has shown that combination therapy can provide superior 24-hour BP control. In the ASCOT study, a combination of calcium channel blocker (Amlodipine) and ACE-I (Perindopril) was shown to be more effective than beta-blocker/thiazide in reducing systolic BP variability [3]. This resulted in reduction of stroke and coronary events between the two treatment groups. This approach is similar to the NICE hypertension guideline, which recommended starting with a calcium channel blocker (CCB) or thiazide diuretic for patients 55 years old or older and an ACE-I (or Angiotensin Receptor Blocker if intolerant of ACE-I) for patients below 55 years old. Subsequently if control is suboptimal, a combination of the CCB and ACE-I or diuretic with ACE-I can then be used.

Combination therapy has the combined efficacy of the individual components used at lower dosages and thus with fewer side effects. Furthermore, single pill combination has been shown to improve patient adherence.

It is useful to note that combination of antihypertensive agents have been categorised by the American Society of Hypertension in order of preference as "Preferred", "Average" or "Unacceptable". This recommendation also includes the newest class of antihypertensive i.e. Renin Inhibitors [11].

"Preferred" combinations are ACE-Inhibitor (ACE-I)-Diuretic, Angiotensin Receptor Blocker(ARB)-Diuretic, ACE-I-Calcium channel blocker(CCB) and ARB-CCB.

"Average" combinations are betablocker-diuretic, CCB (dihydropyridine)-betablocker, CCB/diuretic, Renin-inhibitor-diuretic, Renin-inhibitor-ARB, Thiazide diuretic-Potassium sparing diuretic.

"Unacceptable" combinations are ACE-inhibitor-ARB, ACE-ihhibitor-betablocker, ARB-betablocker, CCB (nondihydropyridine)-betablocker, centrally acting agent-beta blocker.

Ultimately, the choice of therapy also depends on patient factors such as tolerability and cost.

CONCLUSIONS

Optimal hypertension care should include BP monitoring to provide the clinician with a comprehensive BP profile of the patient. To this end, ABPM and HBPM have complementary roles. This approach draws the clinician's attention to particular area of vulnerability for each patient. Together with wider and better choices of antihypertensive agents, especially combination therapies with proven efficacy, the clinician is able to achieve better and more individualised care for hypertensive patients.

Illustrations

Figure 1. 24 –hour Ambulatory BP Monitoring of a patient with well controlled BP and normal diurnal variation. Note that the BP falls during sleep (arrowed line).

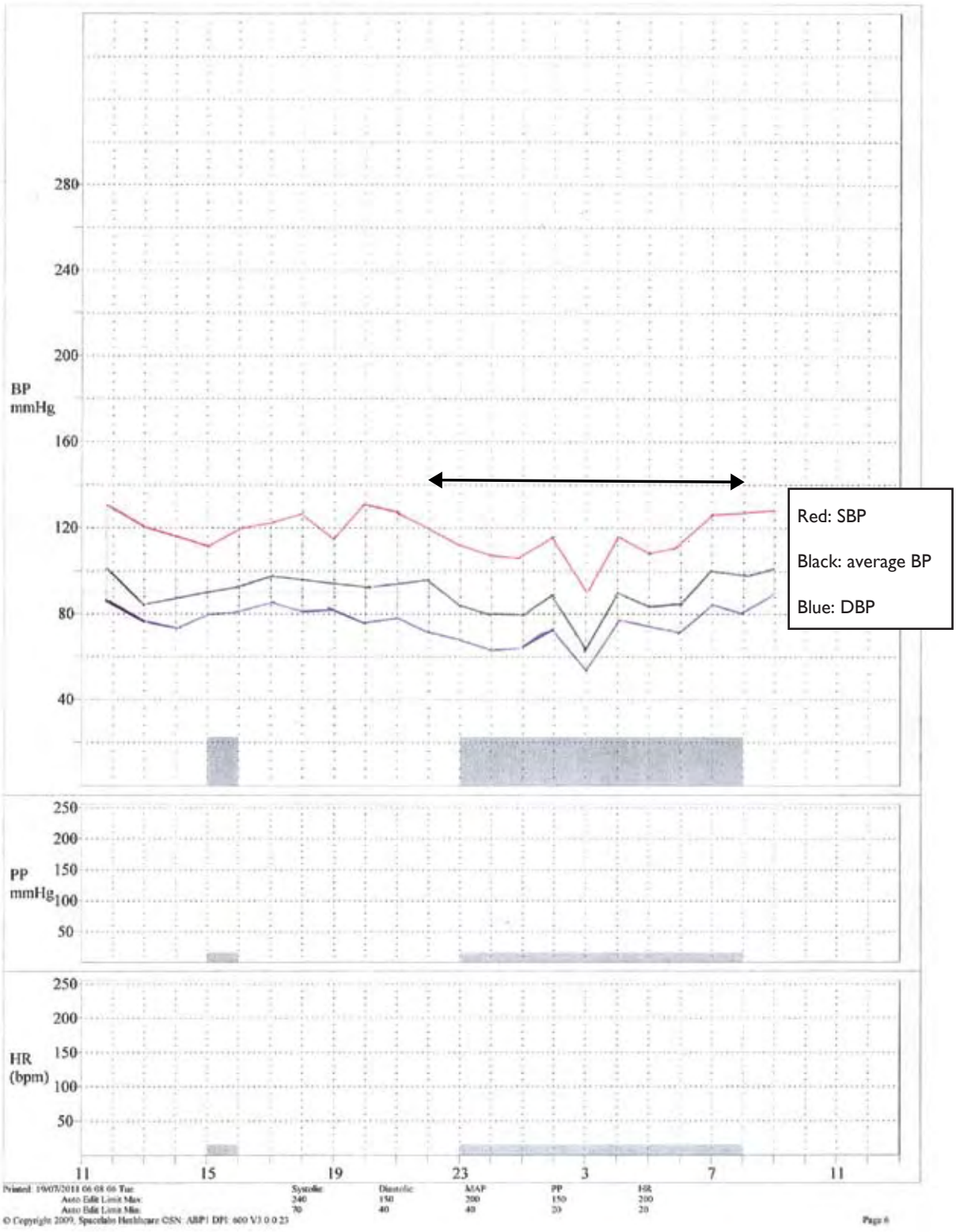
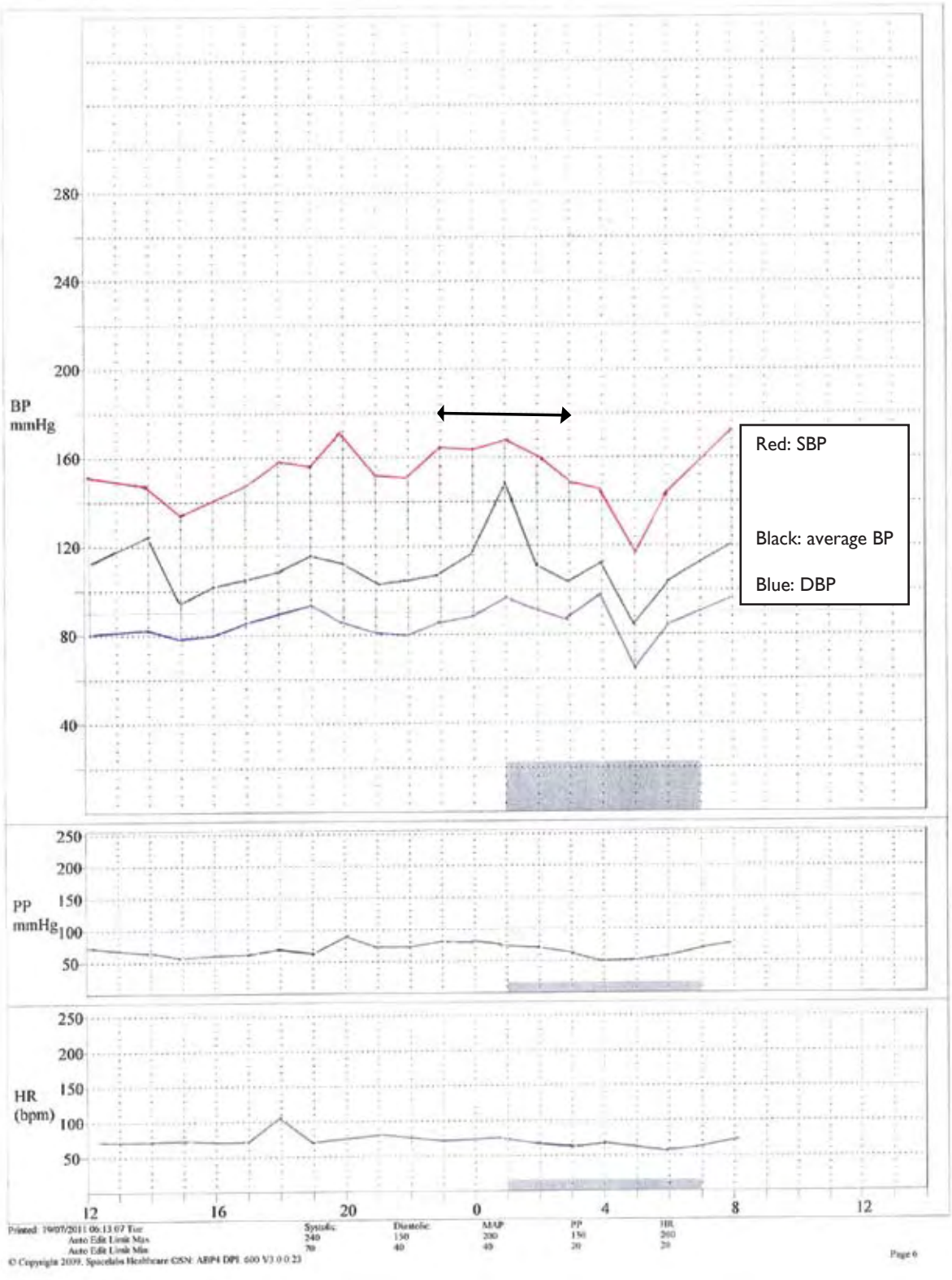


Figure 2. 24 –hour Ambulatory BP Monitoring of a patient whose BP is not well controlled.
There is loss of diurnal variation and BP rises paradoxically during first half of sleep time (arrowed line).



REFERENCES

1. Health Facts Singapore 2010.
2. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for 1 million adults in 61 prospective studies. Lancet.2002;360:1903-1913.
3. Rothwell et al. Effects of beta-blockers and calcium channel blockers on within-individual variability in blood pressure and risk of stroke. Lancet Neurol. 2010;9:469-480.
4. Rothwell et al. Prognostic significance of visit to visit variability, maximum systolic blood pressure and episodic hypertension. Lancet.2010;375:895-905.
5. Pickering et al. Blood Pressure Measurement in Humans: A Statement for Professionals From the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension 2005;45:142-161.
6. Parati et al. ESH Working Group on Blood Pressure Monitoring. J Hypertens 2008;26:1505
7. Verdecchia P. Prognostic value of ambulatory blood pressure : current evidence and clinical implications. Hypertension 2000;35:844
8. Pickering et al. American Society of Hypertension Writing Group. J Am Soc Hypertens. 2008;2:119.
9. Dolan et al. Superiority of ambulatory over clinic blood pressure in prediction of mortality: The Dublin Outcome Study. Hypertension. 2005; 46:156-161
10. Pickering et T. Recommendations for the Use of Home and Ambulatory BP monitoring. American Society of Hypertension Ad Hoc Panel. Am J Hypertens 1996;9:1-11.
11. Gradman AH, Basile JN, Carter BL, et al. Combination therapy in hypertension. J Am Soc Hypertens. 2010;4:42-50.

LEARNING POINTS

- **Optimal hypertension care should include BP monitoring to provide the clinician with a comprehensive BP profile of the patient.**
- **Hypertensive patients who exhibit abnormal BP variability – non-dipper, riser, extreme dipper -- have increased risk of end organ damage and poorer outcome.**
- **The American Society of Hypertension recommends an upper limit of 135/85 mmHg for Home BP**
- **Choice of antihypertensive agents are grouped in order of preference into "preferred combinations", "average combinations", and "unacceptable combinations".**