UNIT NO. 2

HOME BLOOD PRESSURE MONITORING, BLOOD PRESSURE VARIABILITY AND MORNING BLOOD PRESSURE SURGE

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ABSTRACT

Hypertension is a common chronic disease affecting nearly one-third of the adult population and an important predictor of cardiovascular morbidity and mortality. Blood pressure is inherently variable and depends on an individual's physiological state and numerous situational factors. Conventional office recordings to diagnose and monitor a patient's progress and response to treatment is notoriously restrictive. The harmful effects of hypertension are presumed to be due to a prolonged, elevated average BP. Both ambulatory and home blood pressure monitoring are increasingly adopted in clinical practice to eliminate "white coat" and "masked" hypertension and may also be a better prognostic indicator of cardiovascular events than office values. There remain limitations in access and cost to replacing office BP measurements with out-of-office monitoring modalities. Blood pressure also displays a normal circadian variation with nocturnal dipping and a morning surge. Blunted nocturnal dipping and an exaggerated morning surge are thought to correlate with increased cardiovascular events. The pathogenic mechanisms underlying this phenomenon are not well understood. The threshold above which the morning surge becomes pathological is also unclear. More clinical studies targeting treatment of an exaggerated surge are also necessary before clinicians can attribute more weight towards its prognostic importance.

Keywords:
Blood pressure variability; Morning surge; Nocturnal dipping; Ambulatory monitoring;

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INTRODUCTION

Hypertension is the most powerful risk factor for cardiovascular morbidity, including stroke, coronary artery disease, heart failure, chronic kidney disease, and aortic and peripheral arterial diseases.[1,2] While some people experience symptoms, the majority of patients remain asymptomatic. Consequently, hypertension can remain undetected for many years exposing unsuspecting individuals to an increased risk of organ damage and mortality. Primary care physicians manage the majority of hypertensive patients. The principal aims of hypertension management are the improvement in symptoms and reduction of cardiovascular morbidity and mortality.

Accurate understanding of the patient's blood pressure (BP) is essential for both appropriate diagnosis and optimal management. There is marked variability in the blood pressure creating challenges for diagnosis and monitoring response to treatment and long-term outcomes. Office (or clinic) BP measurement may not be the most efficacious index of control and accumulating evidence has shifted the emphasis away from exclusive reliance on office BP measurements to home and ambulatory recordings.

There is marked diurnal variation in the onset time of cardiovascular events, with the peak being exhibited in early morning. Blood pressure also exhibits a similar diurnal variation, with a decrease during sleep and a surge in the morning. A morning blood pressure surge is a normal physiological phenomenon, but several unresolved questions remain on the definition of a pathological surge and the threshold above which constitutes an increased cardiovascular risk.

This article will focus on the role of the following in BP management and their prognostic significance:

1. Home and ambulatory blood pressure monitoring;
2. Blood pressure variability; and
3. Morning surge in blood pressure.

OUT-OF-OFFICE BLOOD PRESSURE MONITORING

1. Home Blood Pressure Monitoring (HBPM)

A large review of 11,502 participants showed 13 percent of individuals display a spuriously high BP reading when it is measured in the office (or clinic).[3] This may be due to anxiety or perhaps a conditional response to the unusual situation. Regardless, these individuals are referred to as "white coat hypertensives". Repeating office BP measurements or asking a nurse/ alternative healthcare professional to measure the BP can partially reduce this white coat effect.

There is clear evidence that out-of-office blood pressure monitoring is superior to the office BP values. Limited accessibility to ambulatory BP monitors (ABPM) or cost concerns has led to the rise in using home BP recordings for diagnostic purposes.

The patient should measure their BP on 7 consecutive days (minimum of 3-4 days) both morning and evening.4 Patients need to be carefully counselled on the method by which the recording is taken, as follows:

- Be seated in a quiet room;
- Have their back and arm supported;
- Be rested for 5 minutes; and
- Take two readings 1-2 minutes apart.

Analysis of these blood pressure recordings should be an

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average of each set of readings, excluding those from the first day.

A 2013 meta-analysis of 52 trials that randomly allocated patients to HBPM or standard clinic-based monitoring found significant benefits associated with home-based monitoring. There was a greater decrease in blood pressure by 3.9/2.4 mmHg at six months in the HBPM arm.[5]

Similarly, other meta-analyses of diverse population cohorts have consistently shown HBPM (both systolic and diastolic values) to have greater predictive value for cardiovascular risk and adverse outcomes, such as stroke, end stage renal disease and mortality, compared to OBP.[6,7] The strengths of these analyses lie in the exclusion of studies that did not adjust for possible confounders such as age, sex and history of cardiovascular disease, meaning the results can be extrapolated on a population level.

Other potential advantages of HBPM include identification of white coat hypertension, assessment of the response to antihypertensive medications, and improvement in patient medication compliance.

2. Ambulatory Blood Pressure Monitoring (ABPM)

Ambulatory blood pressure monitoring machines are worn for 24 hours and take readings every 15 minutes during the day and 30 minutes at night and provide additional information regarding:

- Average day and night readings;
- Blood pressure variability;
- Morning blood pressure surge; and
- Blood pressure load.

The diagnosis of hypertension based upon ABPM depends upon the time span over which it is interpreted:

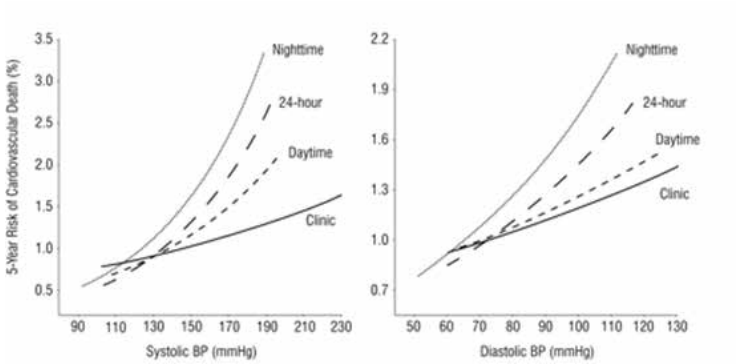
- 24-hour average > 135/85 mmHg;
- Daytime (awake) average > 140/90 mmHg; or
- Night time (asleep) average > 125/75 mmHg.

However, the significance and predictive value of some of these parameters remain unclear.

Evidence from meta-analyses indicates ABPM correlates better to end-organ damage including LVH and increased carotid intima media thickness than OBP.[7]

A population study including more than 5000 participants found that 24-hour ABPM is a better prognostic indicator of mortality and cardiovascular events than OBP (Fig. 1).[8] This study used an Irish population, however these results have been reproduced in other large Asian-based studies.[9]

Figure 1: Adjusted five-year risk of cardiovascular death in the study cohort of 5292 patients for clinic (office) BPM and ABPM. Using multiple Cox regression, the relative risk was calculated with adjustment for baseline characteristics including gender, age, presence of T2 diabetes, history of cardiovascular events and smoking status. The five-year risks are expressed as number of deaths per 100 patients.



(Extracted from Ref 8)

CLINICAL INDICATIONS FOR HBPM OR ABPM

There is no universally accepted list of indications for the use of out of office blood pressure measurements. The ESC practice guidelines are summarised in Table 1.

Table 1: Adapted from the ESC[4]

Clinical indications for HBPM or ABPM
• Suspicion of white-coat hypertension
- Grade I hypertension in the office
- High office BP in individuals without asymptomatic organ damage and at low total CV risk
• Suspicion of masked hypertension
- High normal BP in the office
- Normal office BP in individuals with asymptomatic organ damage or at high total CV risk
• Identification of white-coat effect in hypertensive patients
• Considerable variability of office BP over the same or different visits
• Autonomic, postural, post-prandial, siesta- and drug-induced hypotension
• Elevated office BP or suspected pre-eclampsia in pregnant women
• Identification of true and false resistant hypertension
Specific indications for ABPM
• Marked discordance between office BP and home BP
• Assessment of dipping status
• Suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnoea, CKD, or diabetes
• Assessment of BP variability

Although both HBPM and ABPM overlap with respect to their clinical indications and are equally efficacious in identifying both "white coat" and masked hypertension, there are relative benefits of one BP monitoring modality over the other which are detailed in Table 2. The main advantage of

ABPM over HBPM is the ability to document accurate nocturnal readings and calculate both day and nocturnal averages. There is accumulating evidence that nocturnal BP values are superior to daytime values in predicting mortality.[10]

Some studies have shown HBPM may be as good as ABPM in predicting risk of morbidity/mortality and both are significantly better than OBP.[11] However, it has been suggested by other studies that (although significantly superior to OBP) using HBPM alone for the diagnosis of hypertension would result in substantial over-diagnosis especially for individuals whose recordings are around the diagnostic threshold.[12]

Table 2:

HBPM	ABPM
Readings obtained over prolonged periods of time (weeks and months) in the patient's own environment	Multiple readings obtained within 24 hours allowing more detailed analysis of night and day time readings and blood pressure variability
No need to wear a cumbersome BP cuff for 24 hours which may disrupt sleep	Avoids patient recording error
No need to make multiple clinic visits over 24-48 hours	Results of hypertensive status usually available immediately following the 24 hours.
Avoids misleading BP during activity	Avoids bias in when patients do their BP and better idea of BP during routine activities
Cheaper, more accessible, easier to repeat	

BLOOD PRESSURE VARIABILITY

In healthy individuals blood pressure and heart rate follow a circadian rhythm generated in the suprachiasmatic nuclei of the anterior hypothalamus and mediated by the autonomic nervous system.[13] This allows adaption for higher physiological demands and activity levels while awake.

ABPM helps us understand that the BP is variable throughout the course of the day. Daytime BP, which is when patients are evaluated in the office, can change from hour to hour and is affected by mental and physical activity, stress, and if or when antihypertensive medications were taken. To minimise the influence of office measurement variability, ideally the BP should be measured avoiding known variables such as food intake, strenuous exercise (which can lower the BP), smoking, caffeine consumption up to 30 min prior to the measurement and not talking at the time.

While BP variability from beat-beat, day-to-day and long-term has been studied it is the diurnal variation in blood pressure that has most recently been implicated in the prognosis of hypertension. The mechanisms are not clear but there is reduced arteriolar tone during the night compared to the daytime. Hence, blunted dipping and greater BP values within the large arteries may be transmitted to the microcirculation, facilitating more damage.[10]

The circadian BP rhythm has been extensively studied. There is an early morning fall and clear nocturnal dipping. The decrease in average BP at night is referred to as "dipping". Dipping is generally distributed throughout the population and a decrease of >10 percent of daytime BP is used as the arbitrary cut off to define "normal".[4] There are various reasons for absence of dipping:

- Sleep Disturbance;
- Obesity;
- Obstructive sleep apnoea;
- Orthostatic hypotension;
- Autonomic dysfunction;
- Chronic kidney disease;
- Diabetic neuropathy; and
- Old age.

Several studies have concluded an individual's dipping status to be a predictor of adverse outcomes across different age groups, both men and women, and in both treated and poorly controlled hypertensive patients. A prospective Japanese cohort study reported a 5-percent decrease in nocturnal systolic BP was associated with an 18-percent increase in the risk of cardiovascular mortality.[14] This increased risk was independent of any elevation in the mean 24-hour blood pressure and, interestingly, was also seen in normotensive patients (average 24-hour BP 118/69 mmHg). A similar result was found in a large Western population study where each 10 mmHg increase in mean nocturnal systolic BP lead to a 21-percent increased risk of mortality.[8]

There is only limited data to suggest that nocturnal dosing of antihypertensive medications may restore a dipping pattern.

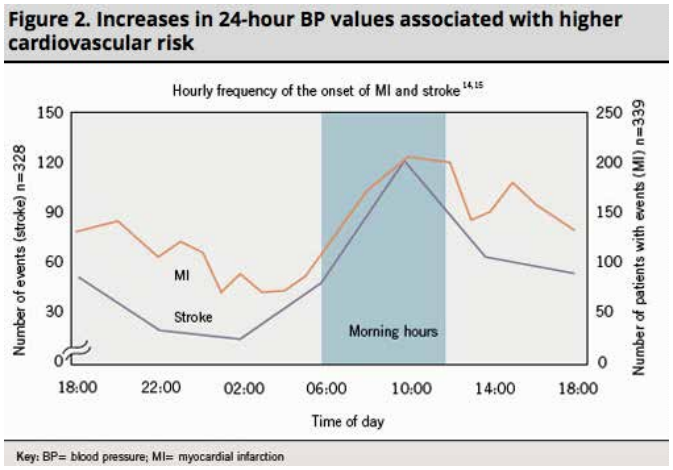
MORNING BP SURGE

Normal morning BP surge (MBPS) is a physiological phenomenon, but an exaggerated morning BP surge is a cardiovascular risk and increased incidence of myocardial infarction and stroke (Fig. 2) and also target organ damage – left ventricular hypertrophy, albuminuria, increased carotid intima-media thickness, arterial stiffness, reduced coronary flow reserve and silent cerebrovascular disease.[16] The association between the degree of the morning BP surge and cardiovascular risk is not linear but rather has a threshold. This threshold at which the MBPS becomes pathological is unclear and this may in part account for many unresolved questions on the pathological significance. The threshold may be modified with age and in the presence of other external stresses (alcohol consumption, poor quality sleep, early morning exercise) and cardiovascular risk factors, such as smoking and obstructive sleep apnoea. One explanation for the observed increase in mortality may be related to repeatedly exceeding the buffering capacity of the larger arteries which may result in structural damage.[17] This may cause plaque rupture by fracturing of the elastin fibres, disorganisation and hypertrophy of the muscular layers of the arterial wall. Atherosclerotic arteries in combination with oxidative stress and older individuals with

impaired baroreflexes may be particularly affected.[17]

Figure 2: Increase in 24-hour blood pressure values and an exaggerated morning blood pressure surge are associated with higher cardiovascular risk.

Hourly frequency of the onset of MI and stroke



(Adapted from ref15.)

A large meta-analysis involving more than 5000 subjects found that both systolic and diastolic MBPS exceeding the 90th percentile are a significant and independent predictor of mortality and cardiovascular events even when other variables such as nocturnal dipping and the 24-hour mean BP level are accounted for.[18] The same meta-analysis suggested that the gradient of rise in blood pressure is implicated in mortality and not the exact value reached.[18] However, the authors stated this hypothesis be "considered with caution" and high-quality epidemiological studies are needed to improve the understanding of the predictive value of MBPS. In contract to these analyses, a large cohort study involving over 3000 individuals found there to be an increased risk of cardiovascular events with a blunted BP surge but no associated risk with an exaggerated MBPS.[19] Due to the normal circadian rhythm causing variations in blood pressure, it stands to reason that a blunting of MBPS represents a pathological response in individuals and therefore predicts risk. The authors of this study could not explain why their results contradict the adverse impact of an exaggerated MBPS observed in many other studies. They suggest this may be due to more stringent adjustments for risk factors such as LVH and eGFR.[19] Alternatively, the lack of any pathogenic association with MBPS may be attributable to it representing only a small proportion of the BP variation that occurs during a 24-hour period.[20]

Hence, several outstanding questions remain for understanding the clinical and prognostic importance of the MBPS compared to other parameters of blood pressure burden. The most important is the lack of a study to test the hypothesis that selective suppression of an exaggerated MBPS leads to the regression of target-organ damage and the reduction of subsequent cardiovascular events. Which class of anti-hypertensive is optimal for reducing the MBPS and its related cardiovascular risk is also uncertain.

CONCLUSION

There is a significant variability in BP level among hypertensives. However, the diagnosis of hypertension and the therapeutic target of BP are based on the average of each BP measured. Accumulating evidence is supportive of the inadequacy of office blood pressure measurements to diagnose hypertension, monitor the response to treatment and long-term follow up of patients with high blood pressure. ABPM monitoring should be considered in all patients before the initiation of life-long pharmacological treatment. HBPM should be thought of as a complementary method of procuring a comprehensive assessment of blood pressure control and is a more accurate predictor of long-term cardiovascular adverse outcomes including mortality.

The morning BP surge is one of the treatable ambulatory BP variabilities and is a potential risk for cardiovascular disease independent of the average of 24-hour BP. Before establishing a clinical practice for patients with morning BP surge, it will be necessary to reach a consensus on the definition and threshold of pathological morning surge. The development of BP monitoring, which more accurately detects the risk of morning BP surge, and a randomised clinical trial offering specific treatments for morning BP surge on cardiovascular events will be needed in the future. The mechanism by which a morning surge and loss of nocturnal dipping incurs adverse risk also needs further exploration.

Much effort is being invested into evaluating the role of chronotherapy and effective 24-hour BP control. It is hoped that by restoring the natural circadian rhythm hypertensive damage can be prevented or regressed.

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LEARNING POINTS

- **Accumulating evidence is supportive of the inadequacy of office blood pressure measurements to diagnose hypertension monitor the response to treatment and long-term follow up of patients with high blood pressure.**
- **ABPM monitoring should be considered in all patients before the initiation of life-long pharmacological treatment.**
- **HBPM should be thought of as a complementary method of procuring a comprehensive assessment of blood pressure control and is a more accurate predictor of long-term cardiovascular adverse outcomes including mortality.**