BLOOD PRESSURE MEASUREMENT

Ambulatory Blood Pressure Measurements in the Management of Hypertension: Practical Importance

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ABSTRACT

Ambulatory blood pressure measurement (ABPM) gives better prediction of cardiovascular morbidity and mortality, and end-organ damage associated with hypertension (HTN) than clinic or casual blood pressure measurements, since the diurnal blood pressure profile and nocturnal blood pressure levels are not ascertained by the later.[1] Although the technology has been available for more than three decades, its role in the evaluation and management of hypertension has been well established only in the past decade. Ambulatory blood pressure measurement is indicated to identify 'white coat' effect/hypertension, masked hypertension, to evaluate drug-resistant hypertension, and to assess adequacy of control in patients at high-risk of cardiovascular disease. The various blood pressure categorizations afforded by ambulatory blood pressure monitoring are valuable for clinical management of high blood pressure and prevention of cardiovascular events. This review summarizes the utility of ambulatory blood pressure monitoring in the management of hypertension and its practical importance.

Keywords: Ambulatory, Blood pressure monitoring, Hypertension.

FUNDAMENTALS OF AMBULATORY BLOOD PRESSURE MONITORING

The first device for ambulatory blood pressure monitoring was developed as early as 1962. It used a microphone taped over the brachial artery, an occlusive cuff which is self-inflated by the patient, and a magnetic tape recorder for recording cuff pressures, electrocardiogram and Korotkoff sounds. A variety of devices are now available for ambulatory blood pressure monitoring, and their pressure detection relies on auscultation, cuff oscillometry or volumetric oscillometry.[2] These three detection

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methods are based on different vascular phenomena during arterial pressure waveform transmission. Auscultatory methods depend on flow and underestimate systolic pressure, whereas oscillometric methods depend on transmitted cuff pressure oscillations, and hence, overestimate systolic pressure. Diastolic blood pressure measurement is inaccurate with finger oscillometry. Most of the current ambulatory blood pressure measurement (ABPM) monitoring devices use an oscillometric method to compute blood pressure (BP) levels so as to eliminate observer bias throughout the day.[2] It is recommended to perform the 24 hours monitoring on a weekday and to obtain a log of activities, wake and sleep duration, timing of drug administration, food intake and occurrence of symptoms, if any. Excessive physical activity during measurements should be avoided. The 24 hours, ABPM provides assessment of the BP including 24 hours average blood pressure load, heart rate, nocturnal dipping and nondipping, trough-to-peak ratio, early morning surge, circadian BP variability, and also the influence of environmental and emotional conditions on BP levels.

ADVANTAGES OF AMBULATORY BP MEASUREMENTS—RECENT EVIDENCES

Several studies have shown that ABPM is as accurate as intra-arterial measurements and mercury column sphygmomanometers.[3] End-organ damage associated with hypertension is more strongly correlated with ambulatory blood pressure than with clinic blood pressure measurements and there is a stronger relationship between left ventricular hypertrophy (LVH) and 24 hours ambulatory systolic blood pressure than clinic systolic blood pressure as shown in many studies.[4,5] A pivotal study by Perloff et al examined eight-year follow-up data of more than 1000 hypertensive individuals who were initially evaluated with both office measurements and ABPM.[6] Ambulatory blood pressure monitoring was found to be an independent prognostic indicator when assessing the overall risk profile of individual patients. Those patients whose ABP values were higher than predicted as compared to their office blood pressure measurements had statistically significant higher cumulative mortality and morbidity (stroke, myocardial infarction) over 10 years, than those

whose ABPM values were lower than predicted. Further, research revealed that among patients with similar office blood pressure measurements, those with relatively higher ABPM values had a greater prevalence of target organ damage, including retinopathy and LVH.[7,8] A prospective study by Imai et al with 1542 subjects and a mean follow-up of 6.2 years has reported that ABP measurements give better prediction of clinical outcomes as compared to conventional clinic or office blood pressure measurements.[9] Mancia et al followed up hypertensive patients for 1 year and showed that ABP monitoring better predicted antihypertensive treatment-induced regression of left ventricular hypertrophy than the clinic blood pressure.[5] Systolic hypertension in Europe (Syst-Eur) trial sub-study (808 participants aged over 60 years with isolated systolic hypertension followed up for a mean of 4.4 years) showed that ambulatory systolic BP was a significant predictor of cardiovascular risk than clinical BP values in elderly subjects with untreated isolated systolic HTN.[10] Ohkubo et al in a prospective study of 1,464 subjects and a mean follow-up of 6.4 years, and Hara et al in 1,007 subjects, showed that 24 hours ambulatory BP was significantly better related to stroke risk and silent cerebrovascular lesions respectively when compared to the clinic BP values.[11,12] Nocturnal BP was the strongest predictor of silent cerebrovascular events.

RECOMMENDATION FOR A SATISFACTORY ABPM

Since, there are no firm data, a satisfactory ABPM recording should have ≥ 70% of expected measurements which is determined by the sleep/awake periods and by the frequency of measurements selected for each period. The present international consensus recommends a minimum of 20 daytime measurements and a minimum seven measurements at night with the interval of measurements being 30 minutes, or more frequently throughout the entire 24 hours period. Daytime and night-time intervals are defined by individual users' diary of sleep and awake times. Daytime is defined as between 0900 and 2100 hours and night-time between 0100 and 0600 hours by discarding transition periods between daytime and night-time. Two valid daytime and one valid night-time measurement per hour is mandatory for research purpose.[13,14] The algorithm for interpretation of results of ABPM in untreated subjects is shown in Flow Chart 1.

HOME BLOOD PRESSURE MONITORING

Home blood pressure monitoring (HBPM) is an alternative to 24 hours ABPM, as it correlates with target organ damage and cardiovascular outcomes more strongly than the clinic

Flow Chart 1: Algorithm for interpretation of results of ambulatory blood pressure monitoring in untreated subjects
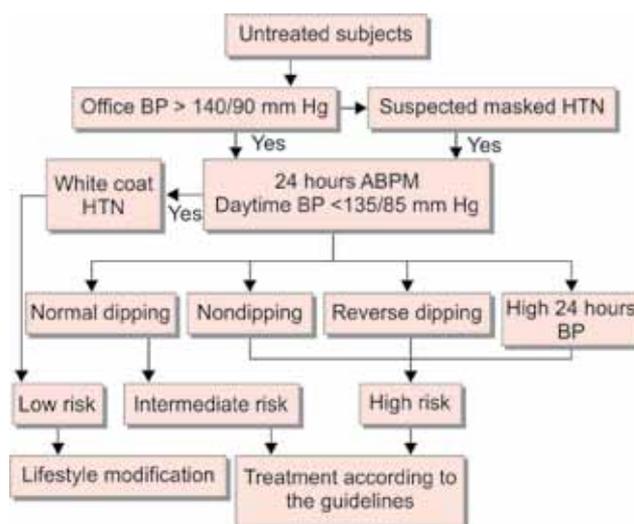
BP measurements.[15-17] Unlike ABPM, it does not allow the assessment of BP round the clock including short-term BP variability. A recent meta-analysis by Hodgkinson et al showed that HBPM and clinic BP measurements are less sensitive and specific when compared with 24 hours ABPM for diagnosing hypertension (HTN).[18] Home BP monitoring should be complementary with ABPM in BP assessment so as to facilitate follow-up of treated HTN patients.

Indications for ABPM[19-21]

- 'White-coat' hypertension (WCH) in patients with newly detected HTN and no evidence of end-organ damage
- Borderline or labile hypertension
- Patients with poorly controlled BP, despite using appropriate antihypertensive therapy
- Patients with worsening end-organ damage, despite adequate office blood pressure control (masked hypertension)
- Suspected nocturnal hypertension and nondippers
- To assess adequacy of 24 hours BP control in patients at high-risk of cardiovascular events (diabetes mellitus, coronary artery disease, peripheral vascular disease)
- Elderly patients with HTN
- Patients with episodic HTN
- Hypertension in pregnancy
- Patients with suspected or confirmed sleep apnea
- Patients with suspected syncope or orthostatic hypotension.

White-coat Hypertension

White-coat hypertension is defined as a clinic BP of 140/90 mm Hg or higher on at least three occasions, with at least two measurements in nonclinic settings being less

than 140/90 mm Hg, without evidence of target-organ damage. The diagnosis of WCH is important because such patients are unlikely to benefit from antihypertensive-drug treatment. Prevalence of WCH increases with age, and may be higher in women compared to men.[22] White-coat hypertension may be present in 20% of subjects who have HTN and in 33% of the diabetic patients.[23] Drug treatment of WCH reduces the clinic blood pressure, but has a negligible effect on the ABP.[24] The cardiovascular risk of patients with WCH is relatively low, and studies have shown that the risk of these patients is similar to the risk of normotensive subjects except in diabetic patients, as the risk of developing true HTN is higher in such groups.[25-27] When office BP levels and ABPM are elevated to the same extent, a diagnosis of true HTN should be made, if the ABPM is normal a diagnosis of WCH can be made. If the ABPM is normal in a treated hypertensive patient, it is defined as 'treated normalized HTN'.[28] White-coat hypertension is also associated with risk of developing diabetes, weight gain and dyslipidemia.[29,30] The rate of conversion of WCH to sustained HTN are higher in older age, overweight and a high salt diet. It is reasonable to recommend life style improvement for those with WCH and all those at higher risk for future cardiovascular disease. Annual surveillance by ABPM is a reasonable approach in those with high-risk of WCH and may be cost-effective to predict those who will develop sustained HTN.[31,32]

White-coat Effect

White-coat effect is defined 'when office BP is elevated and ABPM levels are less elevated than office levels in a hypertensive patient, irrespective of the daytime ABPM level or the use of antihypertensive drugs, and is a recognized cause of resistant hypertension'. An office BP $\geq$ 20 mm Hg systolic or >10 mm Hg diastolic higher than the awake ambulatory BP should be designated as having a clinically important white-coat effect.[33] It may occur more frequently in women than in men. Many patients with resistant HTN, on the basis of their office BP measurements, have controlled BP when assessed by ABPM. In a study, by Brown et al 600 patients with uncontrolled office BP (i.e. >140/90 mm Hg), approximately 60 to 70% had controlled BP on ABPM.[34] In a Spanish study of more than 8200 patients with resistant HTN, 38% were attributed to white-coat effect according to ABPM.[35] Thus, ABPM is indicated for patients with suspected resistant HTN before increasing the doses of medications or adding additional BP lowering medication.

Masked Hypertension

Pickering et al have proposed the term of 'masked hypertension' to denote BP elevation which is determined by ABPM.[36] The phenomenon is suspected in subjects with intermittent raised office BP, family history of HTN in both parents, patients with multiple cardiovascular risks, and diabetic patients.[37] Masked HTN is defined when office BP levels are normal in an untreated subject with an elevated ABPM levels. This condition is present in 10 to 20% of subjects, who are normotensive according to office BP measurements.[38] Several studies have shown that the cardiovascular risk in patients with masked HTN is similar to the risk in patients with sustained HTN.[39,40] This condition should be identified and treated adequately. Hence, ABPM should be done in normotensive subjects who have evidence of target organ damage (LVH, renal failure and microalbuminuria), those with intermittent elevated office BP readings, and those with exaggerated BP response to exercise.[41,42] A study of patients with treated HTN showed that about 33% had masked HTN, and over a five-year follow-up period, their relative risk of cardiovascular events was 2.28 as compared to the patients with adequately controlled BP.[43] Masked HTN in patients with untreated HTN is associated with an increased rate of target-organ damage and an adverse prognosis.[44] Left ventricular mass index and carotid plaque in patients with masked HTN are similar to those with sustained HTN.[45,46] A meta-analyses of several studies including a total of 11,502 participants, with a mean follow-up of 8 years, showed a two-fold higher incidence of cardiovascular disease events in people with masked HTN as compared to those with normal blood pressure.[39] Shimbo et al showed that 83.8% of patients with masked HTN had prehypertension, and 34.1% with prehypertension had masked HTN.[47] Antihypertensive treatment may be warranted in patients with masked HTN, but there are currently no randomized trials or guidelines to recommend management strategy at present.

Nocturnal Blood Pressure

Nocturnal blood pressure is one of the most important measures of the circadian variation during which BP decreases (dips), such that average sleep BP is lower than average awake BP. Ambulatory blood pressure monitoring is the best method for assessing BP variations during sleep. The definition of dipping status is based on the changes in BP from wakefulness to sleep, and it depends on whether the BP falls, rises or remains constant. Physiologically, BP decreases during nighttime (asleep). It is generally agreed that a nocturnal BP fall >10% of daytime values, corresponding to a night/day BP ratio >0.9, serves as a cutoff to define subjects as dippers. When BP falls by <10% during night-time, so that BP does not reach basal levels during sleep, it is defined as nondipping, or occasionally BP increases above daytime average (reverse dippers) (Graphs 1 to 3).[41]

Approximately, 70% of individuals show reduced BP at night (i.e. show dipping) and 30% have nondipping patterns. Nondippers and reverse dippers are associated with increased risk of target-organ damage including stroke, cardiovascular events and death.[48,49] Nondipping is common in diabetic patients with a prevalence of about 30%.[50] The reasons attributed are associated obstructive sleep apnea, autonomic neuropathy and salt retention due to diabetic nephropathy and heart failure.[51] This BP fall is quantified by the day and night-time as noted in subject's diary, or by wide or preferably narrow-fixed time intervals. It is important to relate night-time readings with the patients' diary and associated decrease in heart rate, which is typical in sleep time. Extreme fall of >20% in BP during sleep time is known as extreme dipping which may be associated with mild cognitive impairment in the elderly.[52] Nocturnal BP is superior to daytime pressure in predicting outcome as shown in studies.[48,53] Ambulatory blood pressure monitoring alone can diagnose isolated nocturnal HTN which has a prevalence of about 7% in hypertensive subjects.[54] An increased risk of cerebral hemorrhage was observed in subjects with a large early morning surge of >25 mm Hg and in extreme dippers (those with >20% nocturnal decline in BP), than in normal dippers (those with 10–19% decline).[55] American diabetes association recommends the administration of more than one antihypertensive medications at bedtime.[56]

Ambulatory Blood Pressure Measurement and Management of Hypertension

Twenty-four hours AMBP help us to evaluate the efficacy of drug therapy in decreasing the sleep BP to therapeutic target levels in nondippers.[57] Bedtime antihypertensive drug is indicated in patients with a nondipping pattern, while it should be avoided in extreme dippers. Ambulatory blood pressure monitoring identifies patients with morning BP surge and selects the appropriate drug that control BP throughout the early morning hours, since it reduces the cardiovascular risk associated with the morning BP surge.[55,58,59] Drugs with long-lasting effect in the morning and short-acting agents at bedtime maybe an ideal combination for nondipping patients with morning
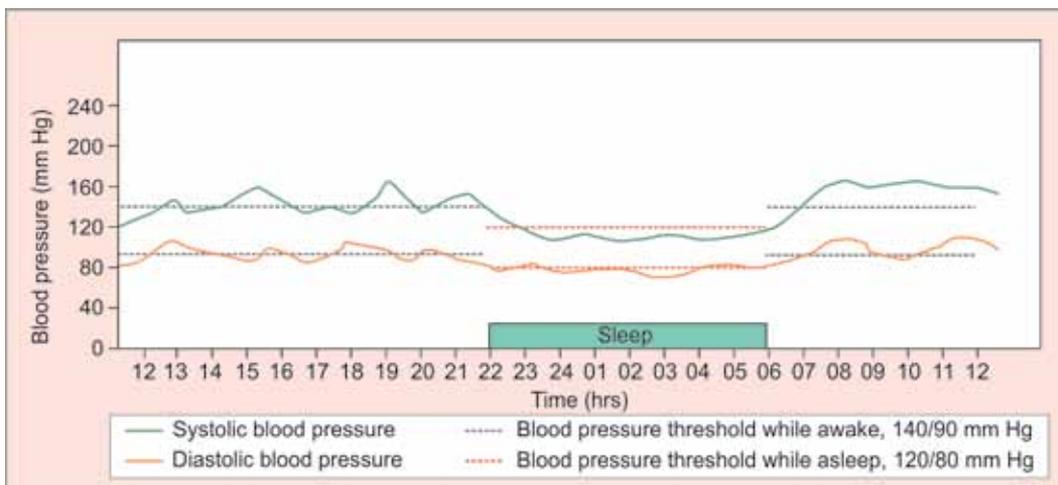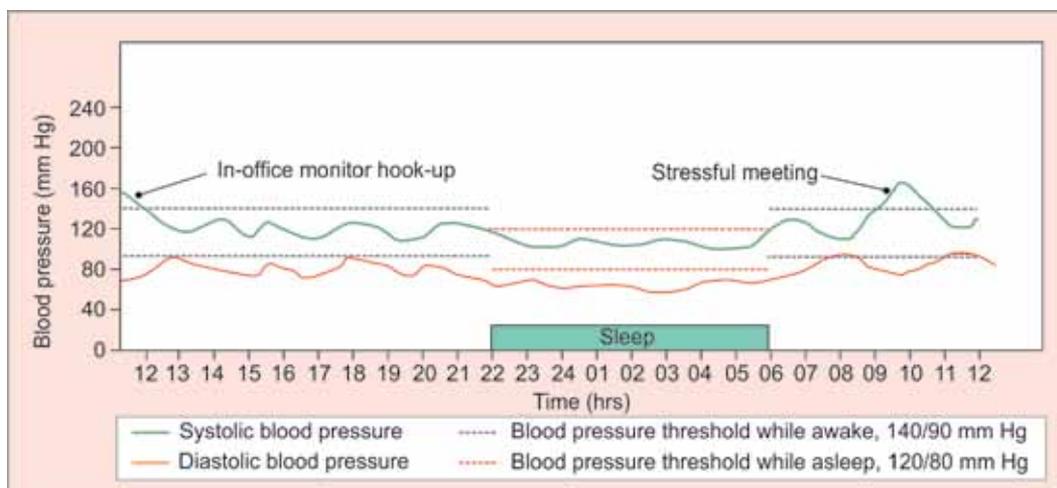

Graph 1: Ambulatory BP report of a hypertensive patient who is a 'dipper'
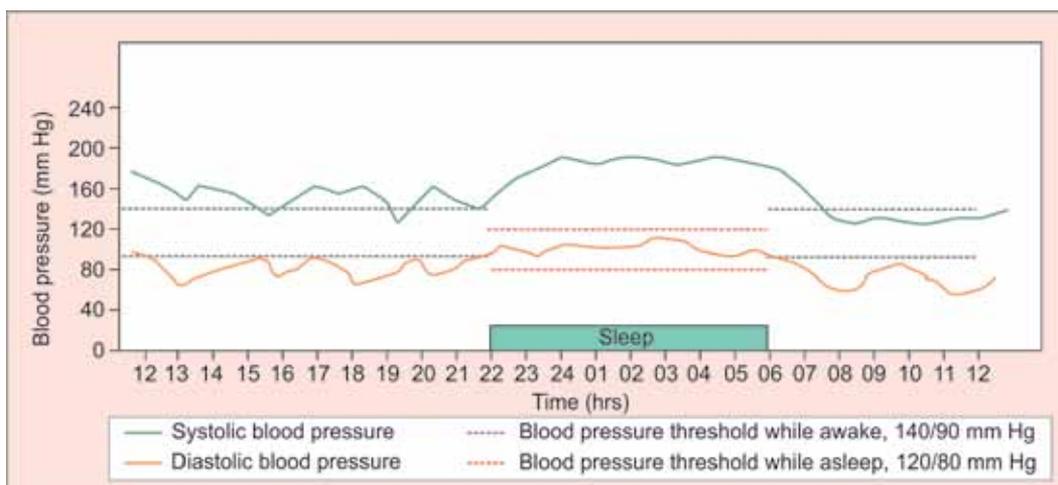
Graph 2: Ambulatory BP report of a hypertensive patient who is not a 'dipper'

Graph 3: Ambulatory BP report of a patient with white-coat hypertension

BP surge, or alternatively administer treatment at night as shown by Hermida et al in hypertensive patients associated with type two diabetes.[60] Ambulatory blood pressure monitoring may help to identify the etiology of secondary HTN in patients with sleep apnea, patients with resistant HTN to exclude white-coat effect and to diagnose the cause of syncope due to orthostatic hypotension, so as to facilitate the selection of right choice of BP lowering therapy.[61,62]

Target Organ Damage

End-organ damage associated with HTN is more strongly correlated with ABP than with clinic blood pressure measurements.[63] Asmar et al found a closer association between arterial stiffness (assessed by carotid-femoral pulse velocity) and ambulatory BP as compared to the office BP.[64] The European lacidipine study on atherosclerosis demonstrated that carotid artery wall status, as demonstrated by the number or size of the plaques, is more closely correlated with 24 hours average systolic BP and ambulatory pulse pressure than the corresponding office values or the lipid profile.[65] Progetto ipertensione umbria monitoraggio ambulatoriale (PIUMA) sub-study demonstrated that the changes in left ventricular mass during BP-lowering treatment was significantly associated with the changes in 24 hours systolic BP, diastolic BP and pulse pressure, and weakly associated with the changes in clinic BP.[66]

Twenty-four hours ABPM and Cardiovascular Risk Prognostication

A lot of informations provided by ABPM have been assessed as prognostic factors. Mean 24 hours daytime and night-time BP values are the principal components of the ambulatory BP, and several studies have shown that the adverse effects of HTN are related to the average

ABP level to which target organs have been exposed over time;[68] the reference values are average 24 hours BP < 130/80 mm Hg, average awake BP (daytime) < 135/85 mm Hg and average asleep BP (night-time) < 120/70 mm Hg. Blood pressure load is the percentage of BP > 140/190 mm Hg by day and >120/80 mm Hg at night (Table 1).[67] Nocturnal BP is more important than daytime BP in predicting subclinical organ damage and cardiovascular outcome, particularly in individuals whose nocturnal (sleep) BP remains high.[68] Ambulatory blood pressure monitoring allows assessment of day-night BP changes that allow cardiovascular risk stratification above office BP and other traditional risk markers.[69,70] Ambulatory blood pressure monitoring assess 24 hours BP variability by computing the standard deviation of the mean systolic and diastolic BP values over a 24 hours period or daytime and night-time BP values separately. Some prospective studies have provided evidence that an increase in BP

Table 1: Average ambulatory BP levels

Blood pressure measure	Normal	Borderline	Abnormal
Systolic average (mm Hg)			
Day	< 135	135–140	> 140
Night	< 120	120–125	> 125
24 hours	< 130	130–135	> 135
Diastolic average (mm Hg)			
Day	< 85	85–90	> 90
Night	< 70	70–75	> 75
24 hours	< 80	80–85	> 85
Systolic load (%)			
Day	< 15	15–30	> 30
Night	< 15	15–30	> 30
Diastolic load (%)			
Day	< 15	15–30	> 30
Night	< 15	15–30	> 30

variability independently predicts cardiovascular events and cardiovascular mortality.[71,72] Ambulatory mean BP and pulse pressure predicts cardiac and cerebrovascular complications more effectively than office BP, and pulse pressure was the dominant predictor of cardiac events, while mean BP was the major independent predictor of cerebrovascular events.[73] Cardiovascular events follow a circadian pattern with a peak incidence in the early morning and a nadir during the night.[74,75] An international database of ABP in a large sample of 5645 subjects and an average 10 years of follow-up revealed that morning surge in BP exceeding the 90th percentile was a significant and independent predictor of all-cause mortality ($p = 0.004$) and cardiovascular events ($p = 0.01$).[76] High heart rate is an important risk factor for cardiovascular and noncardiovascular death. Total and noncardiovascular mortality, with the exception of stroke were relatively higher, with a blunted reduction or an increase in sleeping heart rate and decreased with more nocturnal fall in heart rate.[77,78]

LIMITATIONS OF ABPM

Although ABPM is a useful tool in the management of HTN, patients with very high BP find the cuff pressure uncomfortable, and few report sleep disturbances. Complications with ABPM are rare but include petechia of the upper arm, contact dermatitis, olecranon bursitis, superficial thrombophlebitis and neuralgia. Ambulatory blood pressure monitoring is less accurate when measured during exercise, driving or during an arrhythmia. Ambulatory blood pressure monitoring recording is generally considered unacceptable if less than 85% of

ABPM readings are suitable for use in BP analysis. There is no consensus as to which ABPM measurements (mean 24 hours, daytime or night-time BP) should be used to determine the initial diagnosis, prognosis, evaluation of antihypertensive efficacy, dosage adjustment, and long-term follow-up.[79] The advantages and limitations of ABPM are further elaborated in Table 2.

CONCLUSION

Ambulatory monitoring can be regarded as the gold standard for the prediction of cardiovascular risk over and above conventional office BP measurement, traditional risk factors as shown in several studies and its utility in clinical practice is steadily increasing. Ambulatory blood pressure monitoring is useful when diagnosis of HTN is uncertain, to categorize various types of HTN and to evaluate the efficacy of antihypertensive drugs. It is evident that the additional costs incurred from ABPM are counterbalanced by cost savings from better targeted treatment. Current guidelines recommend ABPM in selected hypertensive patients and should not be adopted routinely in all subjects. Further randomized controlled studies, which compare outcomes in patients with HTN who are treated on the basis of 'ABPM *vs* casual BP measurements', are needed to reinforce the efficacy of ABPM. Ambulatory blood pressure monitoring is an indispensable investigation in patients with established or suspected HTN.

Table 2: Advantages and limitations of ABPM

Advantages	Limitations
• Provides multiple blood pressure measurements	• Patient discomfort
• No observer error and bias	• Cost of technology
• Measures blood pressure during usual activities of daily living and during sleep	• Disturbance of work or sleep
• Evaluate circadian BP variation	• Limited normative data
• Correlates better with end organ damage	• Limited diagnostic and therapeutic guidelines
• Identify white-coat hypertension	• Loss of data due to technical issues
• More reproducible than clinic blood pressure	
• No 'placebo' effect	
• Information on blood pressure variability	
• Evaluation of response to treatment	

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