Review Article

Ambulatory Blood Pressure Monitoring for the Effective Management of Antihypertensive Drug Treatment

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ABSTRACT

Purpose: This purpose of this article is to review the current recommendations for ambulatory blood pressure measurement (ABPM) and the use of ABPM in assessing treatment.

Methods: We review current international guidelines and undertake a critical review of evidence supporting the clinical use of ABPM in effectively managing antihypertensive drug treatment.

Findings: Current guidelines emphasize the diagnostic superiority of ABPM, mainly from the ability of the technique to identify sustained hypertension by allowing for the exclusion of white-coat hypertension and by demonstrating the presence of masked hypertension. ABPM also offers diagnostic insights into nocturnal patterns of blood pressure, such as dipping and nondipping, reverse dipping, and excessive dipping, and the presence of nocturnal hypertension; although less attention is given to the nocturnal behavior of blood pressure in clinical practice, the nocturnal patterns of blood pressure have particular relevance in assessing the response to blood pressure–lowering medication. Surprisingly, although the current guidelines give detailed recommendations on the diagnostic potential and use of ABPM, there are scant recommendations on the benefits and application of the technique for the initiation of blood pressure–lowering therapy in clinical practice and virtually no recommendations on how it might be used to assess the efficacy of drug treatment.

Implications: In view of a deficiency in the literature on the role of ABPM in assess the efficacy of drug treatment, we put forward proposals to correct this deficiency and guide the prescribing physician on the most appropriate drug administration and dosage over time. (*Clin Ther*. 2016;38:2142–2151) © 2016 Elsevier HS Journals, Inc. All rights reserved.

Key words: ABPM, blood pressure–lowering drugs, clinical practice, guidelines, recommendations.

INTRODUCTION

Ambulatory blood pressure measurement (ABPM) is the measurement method of choice for diagnosing hypertension. The technique is more accurate and more cost-effective than office blood pressure measurement (OBPM) or home blood pressure measurement (HBPM). This article reviews the current recommendations for ABPM and the use of abpm in assessing treatment. We review current international guidelines and undertake a critical review of evidence supporting the clinical use of ABPM in effectively managing antihypertensive drug treatment.

REVIEW OF CURRENT RECOMMENDATIONS FOR ABPM IN CLINICAL PRACTICE

Evidence supporting the clinical use of ABPM

The US Preventive Services Task Force recommendations, which have been published recently,[1] the earlier

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recommendations of the UK National Institute for Health and Clinical Excellence,[2] and the European Society of Hypertension [3] have each carefully examined the evidence on which method of blood pressure (BP) measurement is best: OBPM, HBPM, ABPM. each organization has made recommendations for clinical practice. The US Preventive Services Task Force recommendation is practically identical to the UK National Institute for Health and Clinical Excellence recommendation published in 2011, and this concurrence of international opinion is acknowledged by the recommendation that ABPM (or HBPM if ABPM is declined or not tolerated) should be performed in anyone who has had an elevated BP measurement $\geq$140/90 mm Hg recorded by any method of measurement. The UK National Institute for Health and Clinical Excellence not only performed a detailed survey of the relevant literature on measurement techniques but also conducted a comprehensive cost-benefit analysis and concluded that ABPM was more cost-effective than OBPM or HBPM.[4] The cost-effectiveness of ABPM derives from 3 substantial benefits. first, the technique identities white-coat hypertension in approximately 20% of patients who would have been diagnosed with OBPM as having hypertension and thereby prevents unnecessary and costly medication being prescribed, second, masked hypertension is identified in approximately 10% of the population who would have been diagnosed with OBPM as having normal BP and thereby denied the BP-lowering medication to prevent future cardiovascular events. third, in treated patients, in whom BP might be normal as determined by OBPM, ABPM may reveal masked uncontrolled hypertension, which carries serious adverse consequences, especially for high-risk patients.[5] Although ABPM is more cost-effective than OBPM or HBPM,[4] we accept that the costs of performing the technique (device and nurse and physician time) are considerable, and manufacturers must be encouraged to produce inexpensive, accurate, and user-friendly devices to minimize these financial barriers. The European Society of Hypertension position paper has stated, moreover, that it is now incumbent on each country to provide ABPM services to patients who will benefit from improved management of hypertension as listed in Table I.[3] In addition to the guidelines, many national hypertension societies, such as the Canadian Hypertension Education Program, advocate ABPM for the diagnosis of hypertension. However, none of the guideline publications give definitive guidance on how to use ABPM to initiate and assess the response to antihypertensive drug treatment.[6]

Table I. Clinical indications for Ambulatory Blood Pressure Monitoring Pattern.[3]

Identifying white-coat hypertension phenomena
White-coat hypertension in untreated individuals
White-coat effect in treated or untreated individuals
False resistant hypertension in treated individuals
Identifying masked hypertension phenomena
Masked hypertension in untreated individuals
Masked uncontrolled hypertension in treated individuals
Identifying abnormal 24-hour blood pressure patterns
Daytime hypertension
Siesta dipping or postprandial hypotension
Nocturnal hypertension
Dipping status
Morning hypertension and morning blood pressure surge
Obstructive sleep apnea
Assessment of treatment
Increased blood pressure variability
Assessing 24-hour blood pressure control
Identifying true resistant hypertension
Assessing hypertension in elderly people
Assessing hypertension in children and adolescents
Assessing hypertension in pregnant women
Assessing hypertension in high-risk patients
Identifying ambulatory hypotension
Identifying blood pressure patterns in Parkinson disease
Endocrine hypertension

Recommendations for clinical use

The European Society of Hypertension position paper on ABPM, co-authored by leading international experts on BP measurement, is the most comprehensive guideline on the use of the technique.[3]

General recommendations for ABPM in clinical practice

The general recommendations for ABPM in clinical practice should apply also to the use of the technique in therapeutic applications.

Devices

ABPM devices should have been validated independently according to the internationally accepted validation protocols, the most popular of which is the European Society of Hypertension International Protocol.[7] It is also true that recommendations for ABPM use have tended to concentrate on the accuracy of device hardware, with little attention being paid to the software presentation and analysis of ABPM data, features that may be of particular relevance when assessing the response to treatment. Unfortunately, the practicing physician, who has to interpret the considerable amount of data provided by ABPM, is often faced with superfluous detail presented in plots and histograms that have little relevance for clinical practice. The software should be able to provide a standardized plot format on 1 page, with different windows of the 24-hour period identified and normal bands clearly demarcating the individual's awake and asleep intervals. The data should include summary statistics for time-weighted systolic and diastolic BP and heart rate in the windows of the 24-hour period and separately for the awake and asleep subperiods, with the respective SDs and the number of valid BP readings included in the analysis. To remove the variance associated with ABPM interpretation by human observers and to simplify the evaluation of results in routine clinical practice for those unfamiliar with the technique, there should be an automated software-generated interpretative report that indicates normal or abnormal BP patterns, as is currently the case with software-generated ECG reports. The provision of a trend report allowing ABPMs to be compared over time is of particular relevance for monitoring drug treatment so that the response to changes in treatment over time can be readily demonstrated. The system should also be capable of storing data for detailed analysis for research and audit while also facilitating the establishment of national registries.[3] Given the advances in software technology, it should also be possible to provide simple treatment prompts on the efficacy or otherwise of prescribed medication. The provision of such ABPM data to patients might serve to improve adherence to medication.[8]

ABPM thresholds

The selection of cut-off values for ABPM normality in the European Society of Hypertension position paper are summarized in Table II with the caveat that these levels may be conservative and further studies are needed to define thresholds more precisely, particularly in high-risk patients.[3] Indeed, the results of the Systolic Blood Pressure Intervention Trial [9,10] may result in lowering these thresholds, but pending further study the present levels serve as a reasonable goal for treatment (Table II).

Table II. Thresholds for hypertension diagnosis based on Ambulatory Blood Pressure Monitoring.[3]

Threshold	Blood Pressure, mm Hg
24-Hour mean	≥130/80
Awake (daytime) mean	≥135/85
Asleep (night-time) mean	≥120/70

Number of ABPM measurements

In clinical practice, a satisfactory ABPM recording should have at least 70% of expected measurements. This figure will be influenced by the duration of daytime (awake) or night-time (asleep) periods and by the frequency of measurements selected for each period (usually at 30 minute but often at 15- or 20-minute intervals). The minimum of daytime measurements should not be <20, with a minimum of 7 measurements at night based on measurements being performed every 30 minutes or more frequently.[3]

USE OF ABPM TO ASSESS TREATMENT

Current evidence and recommendations

The European Society of Hypertension position paper, although giving considerable attention to the diagnostic role of ABPM, has relatively little to say on the use of ABPM for initiating and following the efficacy or otherwise of treatment: "The frequency of repeat ABPM to evaluate the efficacy of antihypertensive medication will be dependent on the severity of hypertension and the response to treatment. In patients with severe hypertension and evidence of target organ damage, BP reduction is urgent and in the initial stages of treatment, ABPM may be required frequently as different drug combinations are introduced and dosage levels are altered. In patients with mild hypertension and no evidence of target organ involvement, ABPM has to be repeated less frequently according to the device availability, the individual patient's needs and preference, and the physician's discretion."[3]

However, the potential benefit of the technique in influencing therapy was acknowledged: "An Irish study in primary care showed that only 12% of patients achieved target BP with office BP compared with more than one-third of patients with ABPM. Furthermore, 38% of patients had a change in their medication as a result of ABPM, 32% had a new medication started, and 14% of untreated patients with elevated office BP, who were candidates for drug treatment, were not started on medication because ABPM was normal."[11]

These brief statements constitute scarcely 1% of the entire European Society of Hypertension position paper, which hardly does justice to the potential benefit of ABPM in assessing treatment efficacy and the likelihood that this feature may well exceed the diagnostic and interpretative benefits of the technique in clinical practice. This omission becomes particularly important in the context of the suboptimal BP control rates, largely based on OBPM, common to so many countries.

The largest study to date on ABPM in primary care comes from Spain, where a nationwide project to promote the use of ABPM in primary care settings was established a decade ago. One analysis of the Spanish database again supports the use of ABPM as a means of gaining greater insight into the subtleties of drug effects on BP.[12] The study found that 700,000 elderly individuals would have been spared medication if ABPM, instead of casual BP, had been performed. On the other hand, the percentage of patients considered eligible for treatment increased by 6% with ABPM, which amounted to 350,000 elderly patients. In this instance, casual BP was masking hypertension, which only became apparent with ABPM. In other words, the individuals who were spared treatment were partly offset by those who would have been deemed eligible to receive treatment, but this occurrence has to be viewed from the perspective of drug treatment being prescribed appropriately. Moreover, the use of ABPM in the Spanish cohort resulted in a marked reclassification of patients. In untreated individuals, 39% were hypertensive using casual BP but only 19% were hypertensive with ABPM, and these individuals would have been reclassified as having normal BP with ABPM. Similarly, in treated patients, 48% were hypertensive using casual BP, but only 24% were hypertensive with ABPM, meaning that half of these patients would have been reclassified as having normal BP with ABPM. Likewise, 6% of untreated participants had normal BP according to casual BP but would be reclassified as being hypertensive with ABPM, and 8% of treated patients who were normotensive with casual BP would have been reclassified as being hypertensive with ABPM. Finally, BP control was influenced by the method of measurement. There was a considerable gap between the percentage of hypertensive patients at BP goal with ambulatory versus casual BP. Among patients eligible for treatment, only 37% had their BP controlled with casual BP, whereas this figure increased to 54% with ABPM. Although this finding indicates that if ABPM was used to asses BP in the community, the degree of BP control appears much better than with casual BP (simply because multiple BP measurements provide a more accurate assessment). The daunting reality is that only half of all Spanish individuals were within the normal range for both casual BP and ABPM and less than half of individuals with elevated casual BP and ABPM were receiving antihypertensive medication.[12]

The concluding messages from the Spanish study are that, compared with casual BP measurement, ABPM led to a reduction in the proportion of older individuals recommended for hypertension treatment and a substantial increase in the proportion of those whose hypertension was controlled. ABPM would reduce misdiagnosis, ensure that the right people are treated with BP-lowering drugs, and reduce the number of patients treated for hypertension. All this means that ABPM can save much money, and the extra costs of providing the technique would be more than offset by cost savings from better targeted treatment. There is a need to emphasize to physicians the superiority of ABPM over OBPM in not only confirming a diagnosis of hypertension but also determining the response to treatment, which ideally is the achievement of normality during the day and the night.

An analysis of ABPM data from the Dublin Outcome Study database illustrates again just how misleading OBPM can be in assessing a response to treatment. In Figure 1, patients with normal clinic BP (130/70 mm Hg) had 4 hypertensive profiles that were masked by normal OBPM. The hypertensive profiles revealed by ABPM in the illustrated instance demand very different management strategies to those that would be implemented on the basis of clinic BP.[13]

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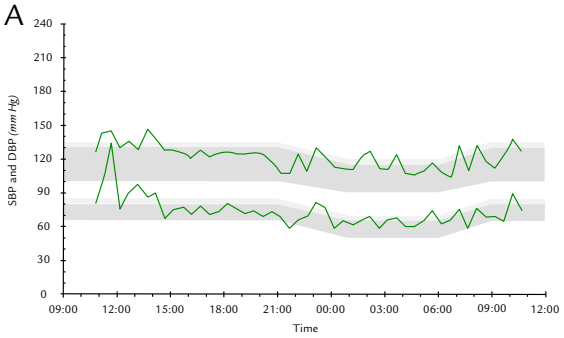

Description	Normal
OBP	150/90 mm Hg
First ABPM Measurement	127/82 mm Hg
Mean Daytime BP	127/77 mm Hg
Mean Night-time BP	115/65 mm Hg

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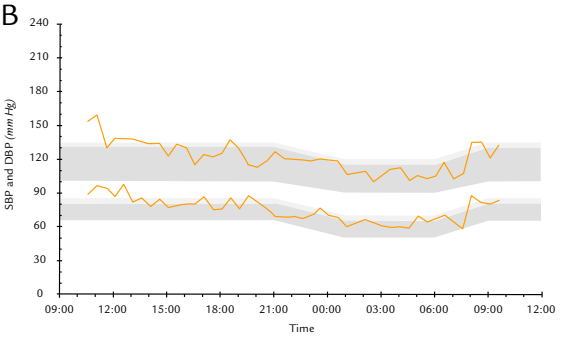

Description	White-coat hypertension
OBP	152/91 mm Hg
First ABPM Measurement	154/89 mm Hg
Mean Daytime BP	128/82 mm Hg
Mean Night-time BP	106/62 mm Hg

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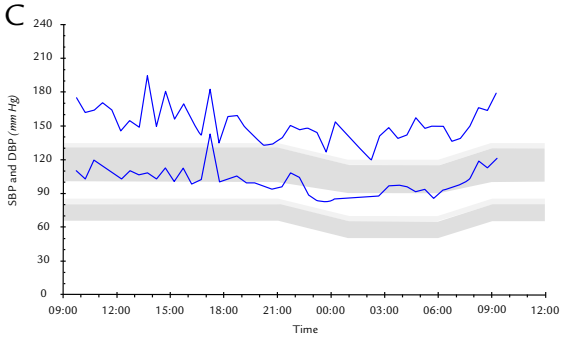

Description	Hypertension with white-coat effect
OBP	152/90 mm Hg
First ABPM Measurement	175/110 mm Hg
Mean Daytime BP	157/107 mm Hg
Mean Night-time BP	142/92 mm Hg

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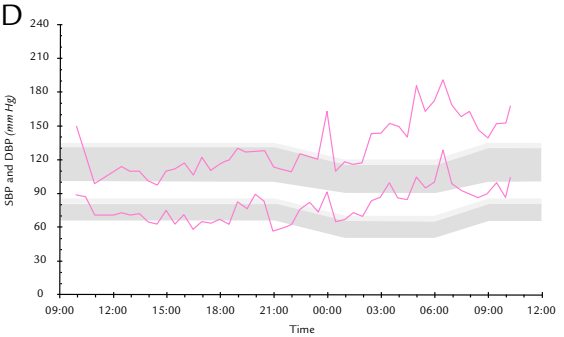

Description	Isolated nocturnal hypertension
OBP	150/90 mm Hg
First ABPM Measurement	150/89 mm Hg
Mean Daytime BP	120/73 mm Hg
Mean Night-time BP	148/88 mm Hg

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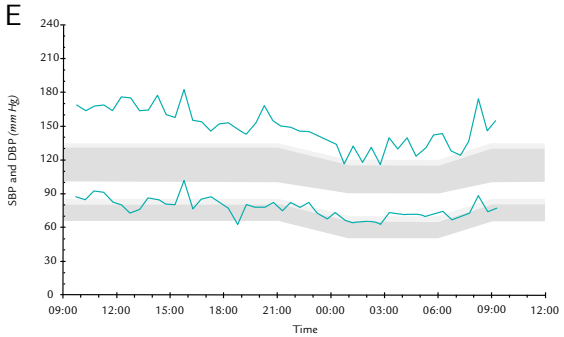
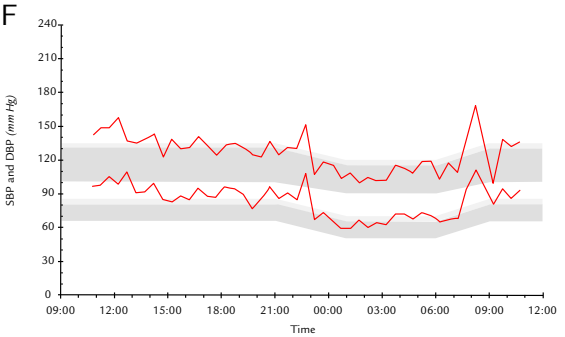


Description	Isolated systolic hypertension
OBP	152/94 mm Hg
First ABPM Measurement	169/87 mm Hg
Mean Daytime BP	160/81 mm Hg
Mean Night-time BP	130/69 mm Hg

F



Description	Isolated diastolic hypertension
OBP	150/95 mm Hg
First ABPM Measurement	142/97 mm Hg
Mean Daytime BP	133/91 mm Hg
Mean Night-time BP	109/67 mm Hg

Figure 1. Examples of ambulatory blood pressure measurements (ABPMs) for which office blood pressure measurements (OBPMs) were all 130/70 mm Hg. BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.

Initiation of treatment

The guidelines are unanimous in recommending ABPM in all patients under consideration for BP-lowering medication. The UK National Institute for Health and Clinical Excellence guideline,[2] the US Preventive Services Task Force recommendation,[1] and the European Society of Hypertension position paper,[3] together with national societies, such as the Canadian Hypertension Education Program,[6] recommend ABPM for all people who have had a BP recording $\geq$140/90 mm Hg by any means of measurement. The rationale behind these recommendations is basically to confirm that the elevation of BP noted on the out-of-office measurement is sustained and not due to a white-coat reaction, as may occur in approximately 25% of patients.[14] A further analysis from the Dublin Outcome Study illustrates just how misleading OBPM is compared with ABPM. As seen in Figure 2, when office BP is within the narrow range of 150 to 152 mm Hg for systolic BP and 88 to 95 mm Hg for diastolic BP, there are no $<$6 diagnostic patterns of BP with ABPM, none of which could be suspected from OBPM. The hypertensive profiles revealed by ABPM in the illustrated instance demand very different management strategies than those that would be implemented on the basis of clinic BP.[13] Indeed, the presence of nocturnal hypertension should prompt consideration of other morbidities, such as secondary hypertension or obstructive sleep apnea. Therefore, as far as the initiation of treatment is concerned, there is no disagreement that ABPM should be offered to all patients before prescribing BP-lowering medication.

Assessing the initial efficacy of treatment

However, we now must move into uncharted waters because the international guidelines have not, as yet, made definitive recommendations on how ABPM should be used in assessing the efficacy or otherwise of prescribed treatment. Of course, the same principles for the use of ABPM in diagnosis will also apply in the use of the technique to monitor and assess the response to treatment. For example, let us assume that we are faced with an untreated patient who has an ABPM pattern like the one in Figure 3. (In this discussion, we are not concerned about the OBPM, but presumably an elevated reading was recorded and was the reason for performing ABPM.) The ABPM reveals significant elevation of both daytime and night-time pressures. Regardless of the patient's risk factor profile, there is increasing evidence that night-time BP predicts outcome over and above other pressures, making it desirable, therefore, to achieve BP reduction throughout the 24-hour period. Of course, if the risk factor profile of the patient is bad (evidence of target organ damage, previous cardiovascular event, bad family history, or comorbidities, such as diabetes), the need to reduce BP becomes more pressing. So once treatment is initiated (and it is not within the scope of this article to discuss how this might be done), it would seem reasonable to repeat ABPM within 2 to 3 weeks to determine whether adequate reduction has been achieved as depicted in Figure 4. If further adjustments in therapy are required, as may indeed be the case, then repeat ABPMs at 2- to 3-week intervals until control is achieved are justifiable.

There is, however, another aspect of treatment that merits consideration, namely, excessive lowering of BP, especially nocturnal pressure. Recent evidence from the Anglo-Scandinavian Cardiac Outcomes Trial ABPM study indicates that, on the one hand, excessive elevation of nocturnal BP carries an adverse cardiovascular risk, but, on the other hand, a group of patients may be adversely affected by excessive lowering of nocturnal BP. In these patients, the vasculature to the heart and/or brain may be compromised by atherosclerotic disease that leaves the patient dependent on a critical level of BP to maintain adequate perfusion, as was indeed enunciated by Floras [15] as long ago as 1988. In the Anglo-Scandinavian Cardiac Outcomes Trial, as in clinical practice, in which treatment was guided by OBPM only, an increase in medication would have excessively lowered BP in a significant number of patients with potential adverse cardiovascular outcome. All of this reinforces the mandatory use of ABPM to both diagnose and follow up patients with hypertension.

Assessing long-term efficacy of treatment

Once control of daytime and night-time ABPM has been achieved (Figure 4), ABPM need only be performed every 6 to 12 months. Systolic BP measurement can be used to obtain confirmatory evidence that BP control is being maintained, at least for daytime BP.[16] However, in substituting HBPM for

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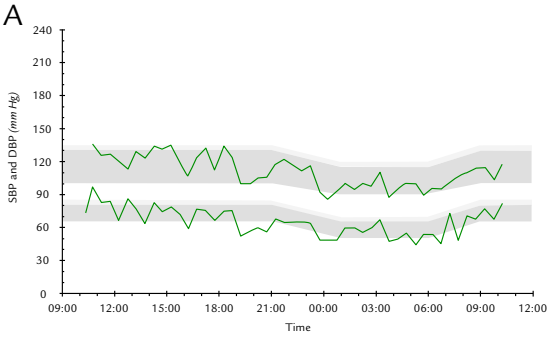

Description	Normal
OBP	130/70 mm Hg
First ABPM Measurement	122/74 mm Hg
Mean Daytime BP	119/71 mm Hg
Mean Night-time BP	98/56 mm Hg

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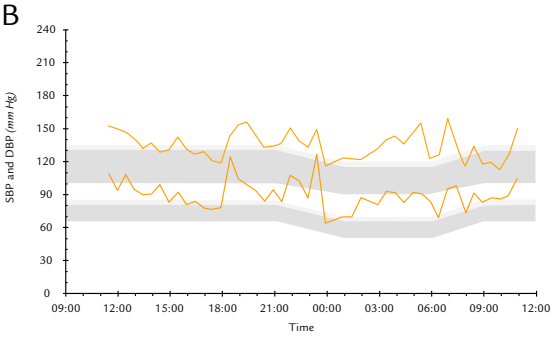

Description	Daytime diastolic and nocturnal hypertension
OBP	130/70 mm Hg
First ABPM Measurement	153/109 mm Hg
Mean Daytime BP	134/91 mm Hg
Mean Night-time BP	135/86 mm Hg

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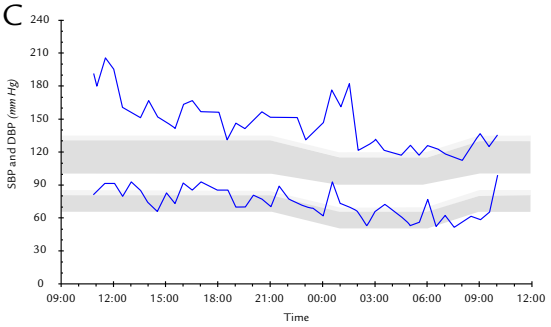

Description	Masked isolated systolic hypertension with white-coat effect
OBP	130/70 mm Hg
First ABPM Measurement	191/81 mm Hg
Mean Daytime BP	152/80 mm Hg
Mean Night-time BP	132/64 mm Hg

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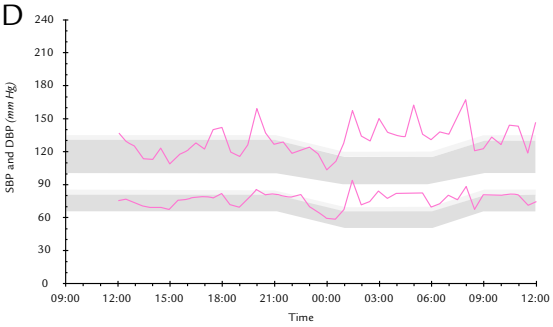

Description	Isolated nocturnal hypertension
OBP	130/70 mm Hg
First ABPM Measurement	137/76 mm Hg
Mean Daytime BP	129/77 mm Hg
Mean Night-time BP	141/80 mm Hg

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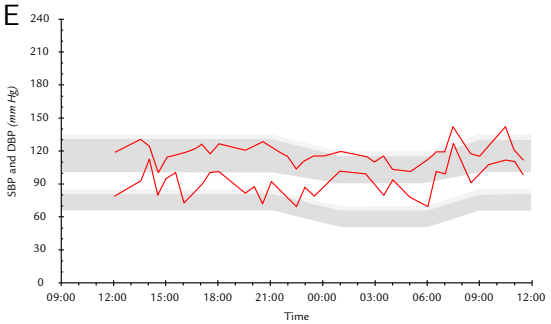

Description	Isolated diastolic hypertension
OBP	130/70 mm Hg
First ABPM Measurement	119/79 mm Hg
Mean Daytime BP	122/94 mm Hg
Mean Night-time BP	110/88 mm Hg

Figure 2. Examples of ambulatory blood pressure measurements ABPMs for which office blood pressure measurements (OBPMs) was 150 to 152 mm Hg systolic blood pressure (SBP) and 88 to 95 mm Hg diastolic blood pressure (DBP). BP = blood pressure.

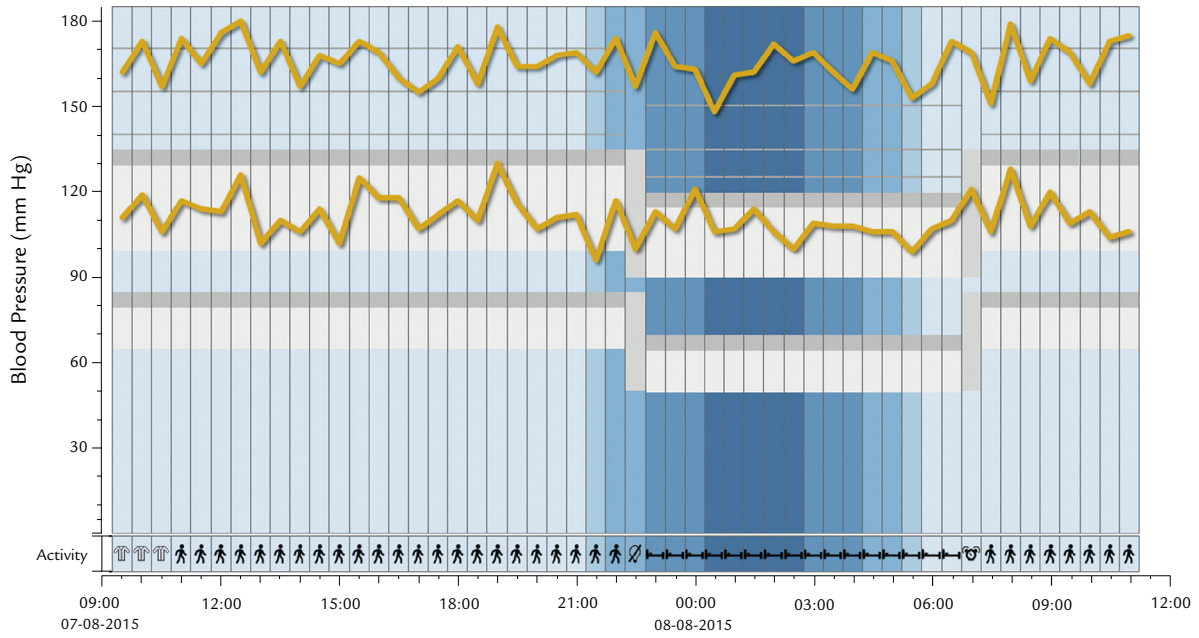

Figure 3. Hypertensive nondipper. The ambulatory blood pressure monitoring pattern reveals significant hypertension during the 24 hours and a reduced decrease in blood pressure during sleep. Plot and interpretive report provided with permission from Medasoft.

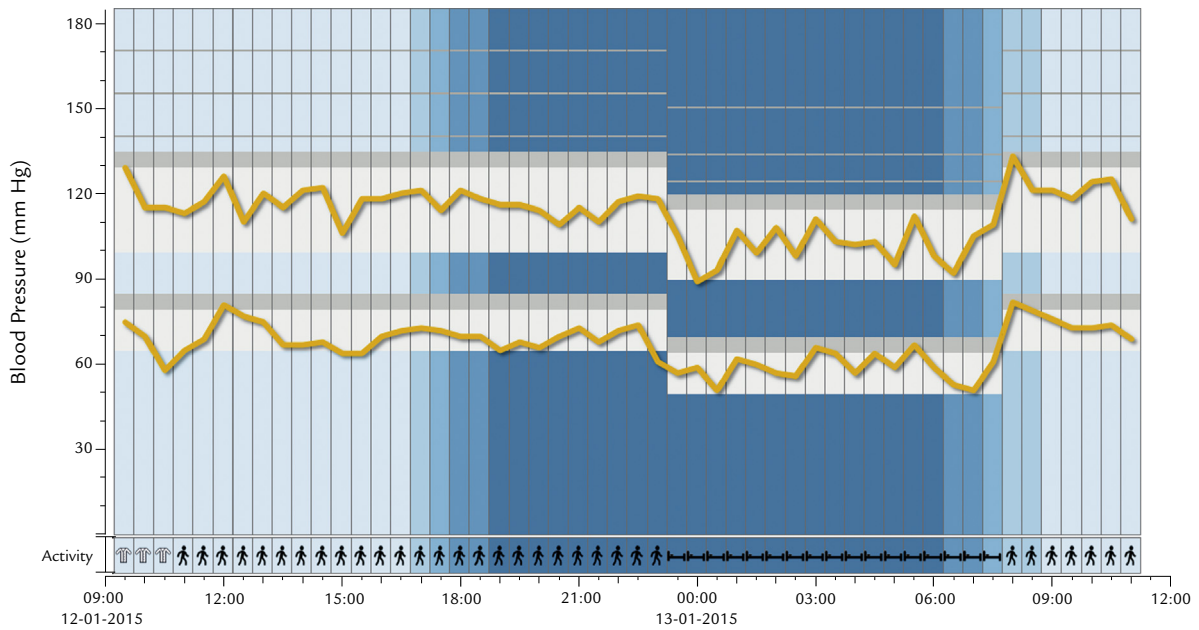

Figure 4. Normal ambulatory blood pressure monitoring pattern. The ambulatory blood pressure monitoring pattern reveals normal 24-hour blood pressure and a normal decrease in blood pressure during sleep. Plot and interpretive report provided with permission from Medasoft.

ABPM, it must be emphasized that to obtain a HBPM equivalent to mean daytime ABPM, it is necessary to obtain the mean of 6 days of systolic BP measurements (2 readings per day) after discarding the measurements from the first day.[3,16] This is regarded by many patients (and physicians) as being more onerous than performing ABPM, which, in addition, provides nocturnal BP measurements, which are increasingly important in assessing BP control.

CONCLUSION

ABPM is now accepted as being indispensable to good clinical practice for the diagnosis of hypertension, mainly to exclude white-coat hypertension and to identify masked hypertension. Although it is recognized that ABPM can also be useful in the therapeutic management of hypertension, there are surprisingly few recommendations on how the technique might be used in this regard. In this article, we have made recommendations on how ABPM might be used to initiate treatment and to assess the efficacy of BP-lowering therapy over time. We recommend, moreover, that the software program used to present the result of the ABPM should be capable of providing trend reports to allow for the ready assessment of treatment efficacy. Evidence is lacking for the use of ABPM to guide treatment in specific groups, other than acknowledgement that high-risk groups, such as patients with chronic kidney disease,[3] are more likely to benefit from having ABPM performed if for no other reason than to determine and treat night-time blood pressure, which is often elevated in such patients. Although the role of ABPM in clinical practice is becoming clearer, we acknowledge that evidence from randomized clinical trials using ABPM to monitor treatment in practice and to determine the benefit of reducing components of ABPM, such as night-time blood pressure, are now needed.

CONFLICTS OF INTEREST

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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