Brief Review

Ambulatory Blood Pressure Measurement
What Is the International Consensus?

Eoin O’Brien, Gianfranco Parati, George Stergiou

The Working Group on Blood Pressure Monitoring of the European Society of Hypertension (ESH) published recommendations for blood pressure (BP) measurement in 2003 and a guideline for home BP measurement in 2008. Ambulatory BP monitoring (ABPM) has become a subject of considerable scientific interest with >10,000 articles listed on PubMed in 2012. In 2001, the Center for Medicare and Medicaid Services in the United States approved ABPM for reimbursement for the identification of subjects with white-coat hypertension, and in 2011, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom recommended that ABPM should be offered as a cost-effective technique to all people suspected of having hypertension.

One of the first meetings to examine the potential of ABPM was held in Ghent in 1978, and since then the ESH Working Group on Blood Pressure Monitoring has held several consensus conferences, the most recent being in Milan in 2011. The technique was comprehensively reviewed and, arising from this meeting, a position article was drafted incorporating the opinions of 34 international experts in hypertension and BP measurement. During the drafting of this article, it became apparent, first, that the large literature on ABPM was in need of assessment but that drafting a systematic review on this topic would be a difficult task, given the very large number of studies dealing with ABPM, and second, that even among experts, there was differing opinion on certain basic aspects of ABPM, such as the definition of white-coat and masked hypertension. In this article, we highlight these areas of potential controversy, not as an indictment of expert opinion but rather to illuminate aspects of the technique in need of clarification, and perhaps, as importantly, in need of further research.

Devices and Software

Most devices available for ABPM have been validated independently according to the internationally accepted validation protocols, the most popular of which is the International Protocol of the ESH. However, whereas this is true for the adult population, evaluation of device accuracy in special populations, such as children and patients with arrhythmias, is not often performed, and the 2013 ESH ABPM Position Paper encourages manufacturers to extend validation to such populations.

Till-date 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. As a consequence, 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 Position Paper breaks new ground, therefore, in stipulating the software requirements for ABPM. 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 demarcated showing the subject’s awake and asleep time 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 the 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 indicating normal or abnormal BP patterns, as is currently the case with software-generated ECG reports, and the provision of a trend report allows ABPMs to be compared over time to demonstrate the response to changes in management. The system should be capable of storing data for detailed analysis for research and audit while also facilitating the establishment of national registries.

ABPM Thresholds for Clinical Practice

The selection of cutoff values for ABPM normality excited much discussion among the authors; however, ultimately the threshold values in the recent NICE guidelines, the JNC 7 (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee) guideline, and the ESH (European Society of Hypertension)/ESC (European Society of Cardiology) guidelines for 2013, and the results of outcome studies, such as IDACO (International Database on Ambulatory blood pressure monitoring in relation to Cardiovascular Outcomes Investigators) and Ohasama, influenced the definition of consensus values summarized in
Table 1. Thresholds for Hypertension Diagnosis Based on ABPM

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Value</th>
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<tbody>
<tr>
<td>24-h Average</td>
<td>≥130/80 mmHg</td>
</tr>
<tr>
<td>Awake (daytime)</td>
<td>≥135/85 mmHg</td>
</tr>
<tr>
<td>Asleep (night-time)</td>
<td>≥120/70 mmHg</td>
</tr>
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ABPM indicates ambulatory blood pressure monitoring.
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Table 2. Evaluation of ABPM Data

Definition of daytime and night-time
Daytime and night-time intervals are best defined using sleeping times reported by individual users’ diary cards (awake and asleep periods)

ADDITIONAL MATERIAL

White-Coat Hypertension
In clinical practice, the most well-established indication for performing ABPM, as recommended in all international guidelines, is to identify untreated patients who have high BP readings in the office but normal readings during usual daily activities outside of this setting, that is, white-coat hypertension, and to identify varying 24-hour BP profiles. The traditional definition of white-coat hypertension is based on an elevated office BP ≥140 mmHg systolic and/or ≥90 mmHg diastolic with a normal BP during the awake period, that is, a mean awake ambulatory systolic/diastolic BP <135 and <85 mmHg in untreated subjects. However, in recent years, there has been increasing interest in BP behavior during sleep, and nocturnal BP is now recognized to be superior to daytime BP in predicting cardiovascular risk. It seems illogical, therefore, to exclude this period in definitions of white-coat hypertension, and the Position Paper proposes including patients with office
Table 3. Clinical Indications for ABPM

| Identification of white-coat hypertension phenomena |
| White-coat hypertension in untreated subjects |
| White-coat effect in treated or untreated subjects |
| False resistant hypertension in treated subjects |
| Identifying masked hypertension phenomena |
| Masked hypertension in untreated subjects |
| Masked uncontrolled hypertension in treated subjects |
| Identifying abnormal 24-h blood pressure patterns |
| Daytime hypertension |
| Siesta dipping/postprandial hypotension |
| Nocturnal hypertension |
| Dipping status |
| Morning hypertension and morning blood pressure surge |
| Obstructive sleep apnoea |
| Increased blood pressure variability |

Assessment of treatment

Increased on-treatment blood pressure variability

Assessing 24-h blood pressure control

Identifying true resistant hypertension

Assessing hypertension in the elderly

Assessing hypertension in children and adolescents

Assessing hypertension in high-risk patients

Identifying ambulatory hypertension

Identifying blood pressure patterns in Parkinson disease

Endocrine hypertension

ABPM indicates ambulatory blood pressure monitoring.

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readings ≥140/90 mm Hg and a mean 24-hour BP <130/80 mm Hg, thereby incorporating nocturnal BP in the definition. Although several hypertension guidelines recommend ABPM when white-coat hypertension is suspected, the basis for selecting patients is somewhat imprecise because there are no characteristics that have a high specificity for diagnosing this condition. Perhaps the best reason to suspect white-coat hypertension is when patients with high office BP report normal BP readings taken at home or in the community. Indeed, a high out-of-office reading to determine whether an elevated office BP is sustained is the primary indication for reimbursement of ABPM by government insurance plans in some countries such as the United States,7 and NICE recommends ABPM for all patients suspected of having hypertension because of a previously elevated office BP measurement,1 whereas the 2013 ESH guidelines recommended ABPM for the detection of white-coat hypertension in low- or moderate-risk patients with elevated office BP.7

With the prevalence of white-coat hypertension in the community being as high as 20% to 25%, it is important to make an accurate diagnosis,14 which can best be achieved by performing 24-hour ABPM and home BP monitoring before prescribing antihypertensive drug therapy. The Position Paper recommends that people with white-coat hypertension should have the diagnosis confirmed in 3 to 6 months and be followed at yearly intervals with ABPM, or home BP monitoring, so as to detect whether and when sustained hypertension occurs. The Position Paper emphasizes that the term white-coat hypertension should be restricted to people who are not on antihypertensive medication.

White-Coat Effect

White-coat effect is defined as the rise in BP that occurs in the medical environment regardless of the daytime ABPM level or the use of antihypertensive drugs. In general, white-coat effect is present when the office BP is considerably higher than the awake ABPM, whereas white-coat hypertension exists if the office BP is high, and the awake ambulatory BP is normal in a patient not receiving antihypertensive medication. White-coat effect is a recognized cause of false resistant hypertension and may be present in anyone treated for hypertension, regardless of the number of drugs being taken. Other patients may have only mild hypertension based on ABPM and yet appear in the office to have severe hypertension attributable to a white-coat effect.

However, it is difficult to see any purpose in classifying patients with only a few mm Hg elevation of office BP above daytime ABPM, and it is recommended that patients with an office BP ≥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.15 In this way, those patients with only a small difference between office and ambulatory BP are not considered as meriting a change in drug therapy. This indication, however, has to be taken with some caution. Indeed, evidence is available that a difference between office and ambulatory BP levels cannot necessarily be ascribed to a white-coat effect. Such an effect can be best quantified by direct recording during an office visit,16 or by considering the BP values obtained during the white-coat window of ABPM.17

Masked Hypertension

The usual definition of masked hypertension is the presence of a normal office BP <140/90 mm Hg with elevated daytime BP on ABPM (≥135/85 mm Hg) or home BP ≥135/85 mm Hg.18 However, as with the definition of white-coat hypertension, it is inappropriate to exclude nocturnal BP; and the definition should be extended to include also 24-hour BP values ≥130/80 mm Hg. Concerning the question as to whether or not the definition of masked hypertension should be applied also to subjects on BP-lowering medication and not only to untreated subjects, the Position Paper considers it inappropriate to apply the term to subjects on treatment because by definition hypertension has been diagnosed and cannot be masked. Therefore, when treated subjects have a normal office BP but persistently elevated ambulatory or home BP, the term masked uncontrolled hypertension is more appropriate. This term acknowledges that poor control of BP with medication during the day or night-time periods, in spite of normal office BPs, may be masked. Patients with this condition should be offered effective therapeutic BP control throughout the 24-hour period to prevent the cardiovascular consequences of uncontrolled hypertension (Table 4). Recent evidence suggests that masked uncontrolled hypertension is particularly common among...
Table 4. Definition of White-Coat and Masked Hypertension Phenomena*

<table>
<thead>
<tr>
<th>Phenomena</th>
<th>Definition</th>
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<tr>
<td>White-coat hypertension</td>
<td>Untreated subjects with elevated office blood pressure ≥140/90 mmHg† and</td>
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<tr>
<td></td>
<td>24-h ABPM &lt;130/80 mm Hg and</td>
</tr>
<tr>
<td></td>
<td>Awake ABPM &lt;135/85 mm Hg and</td>
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<tr>
<td></td>
<td>Sleep &lt;120/70 mm Hg or</td>
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<tr>
<td></td>
<td>Home blood pressure &lt;135/85 mm Hg</td>
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</table>

ABPM indicates ambulatory blood pressure monitoring.
*Diagnoses require confirmation by repeating ABPM or Home BP monitoring within 3–6 mo, depending on the individual’s total cardiovascular risk.
†Ambulatory blood pressure values obtained in the clinic during the first or last hour of a 24-h recording may also partly reflect the white-coat effect.
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phy high-risk patients and is often attributed to isolated nocturnal hypertension, which highlights the major role of 24-hour ABPM in the evaluation of treated individuals with high cardiovascular risk. It is interesting to mention that the UK NICE ignored the usefulness of ABPM in detecting masked hypertension (NICE), whereas the 2013 ESH recommended ABPM for detecting masked hypertension in all subjects with high-normal office BP or normal office BP with asymptomatic organ damage or at high total cardiovascular risk.9

Nocturnal Phenomena

ABPM is the best measurement methodology for assessing BP during sleep. The definition of the so-called dipping status is traditionally based on the behavior of BP on going from wakefulness to sleep, depending on whether BP falls, rises, or remains constant. This BP fall is usually quantified by defining the daytime and the night-time periods based on the subject’s diary (which is the preferred method in many clinical practices), or alternatively through use of wide-fixed or preferably narrow-fixed time intervals. In the former case, the entire 24-hour time is arbitrarily subdivided into awake and asleep subperiods by including all recording hours. In the latter case, transition times between day and night and between night and day are not included in the estimation of day and night average pressures, because of differences in the times when different subjects go to bed or wake up, leading to inconsistencies in bed rest time among individuals, which prevent it from being categorized reliably without a diary. In some patients, the nocturnal decline in BP may be absent (nondipping), so that BP does not reach what could be defined as basal levels during sleep. In some instances, BP may even rise during sleeping hours to reach levels that are higher than daytime levels (reverse dipping or rising). Alternatively, there may be a marked fall in BP during the night window to give the phenomenon of extreme dipping. The magnitude of the rise in BP in the morning around the awakening time may also yield additional prognostic information, and is commonly referred to as the morning surge.19

There is compelling evidence that nocturnal BP is superior to daytime pressure in predicting outcome.20,21 This has led investigators to suggest that the most important parameter for predicting outcome is the level of night-time BP, rather than any measure of day-night BP difference. Isolated nocturnal hypertension, which may be present in 7% of hypertensive subjects, can only be diagnosed with ABPM.22 Nocturnal hypertension in patients participating in antihypertensive drug trials could have an important influence on the evaluation of the 24-hour efficacy of BP-lowering drugs.

Although the degree of night-time dipping (defined as the difference between daytime and night-time BP) has a normal distribution in a population setting, it is generally agreed that a nocturnal BP fall >10% of daytime values, corresponding to a night/day BP ratio >0.9 serves as an arbitrary cutoff to define subjects as dippers.

There are, thus, several patterns of nocturnal BP behavior, and although these may be associated with an adverse prognosis, there has been relatively little study into the benefits of therapeutic modification of nocturnal patterns. Recently, the American Diabetes Association recommended the administration of ≥1 antihypertensive medications at bedtime.23 The Position Paper considers the evidence supporting this recommendation as inadequate based on present evidence but supports the objective that the aim of treatment should be to reduce nocturnal hypertension so as to achieve BP control during the entire 24-hour period.

When to Repeat ABPM in Clinical Practice

The recommendation as to when ABPM should be repeated was debated at length. However, so many factors influence any recommendation that the question largely becomes one of clinical judgment and the availability of ABPM. For example, severe or apparently resistant hypertension, the presence of target-organ damage, the existence of comorbidities, such as diabetes mellitus, and a positive family history of cardiovascular disease should prompt frequent ABPM in the quest for BP control, whereas mild hypertension and the absence of target-organ involvement and other features of cardiovascular disease might call for less frequent ABPM and the use of self-BP measurement at home.2

Role of Home BP

The Position Paper recommends that ABPM should be performed whenever possible in subjects with suspected hypertension, in whom it is necessary to confirm the diagnosis of sustained hypertension (ie, to exclude white-coat hypertension), to assess the severity of hypertension throughout the 24-hour period, to detect nocturnal hypertension, to detect
patterns of BP behavior such as nondipping and alterations in BP variability attributable to autonomic failure, and to be able to analyze the 24-hour data for indices of BP fluctuations, such as the ambulatory arterial stiffness index, and measures of BP variability. ABPM is particularly appropriate for the initial evaluation because it provides standardized and unbiased information within 24 hours and without need of training, skills, and commitment from the patient, as required for home BP.

However, when ABPM is not readily available, out-of-office assessment of BP with self-home monitoring is recommended according to the procedure recommended the ESH guideline by having duplicate morning and evening self-measurements for 7 days and calculating the average after discarding measurements on the first day. Home BP measurement also has a role in monitoring BP control in treated subjects during extended periods of time between office visits, especially in patients with good BP control on ABPM, and there is the added advantage that it can improve long-term adherence to medication and thereby hypertension control rates.24–26

BP Variability

The importance of BP variability, both as an indication for ABPM and in the interpretation of results, was reviewed in the Position Paper. BP is a highly dynamic parameter characterized by continuous fluctuations that include both short- and long-term variability.27 Although short-term BP variability within 24 hours can be readily assessed with ABPM, long-term variability requires repeated BP measurements during days, weeks, or months with repeated office, home, or ABPM.27,28 Although the adverse cardiovascular consequences of hypertension largely depend on average BP values, evidence from observational studies and post hoc analyses of data from clinical trials have indicated that these outcomes may also depend on increased short-term and long-term BP variability.29–32 The issue as to whether or not antihypertensive treatment should be targeted not only toward reducing mean 24-h BP levels but also toward stabilizing BP variability and optimizing cardiovascular protection remains to be answered with prospective intervention studies. Based on the available evidence, short-term BP variability might be considered for risk stratification in population and cohort studies. However, it does not yet represent a parameter for routine use in clinical practice because of the current lack of generally accepted thresholds separating normal from pathological BP variability levels, and because controlled intervention studies are still needed to establish whether a treatment-induced reduction in short-term BP variability will be accompanied by a reduction in cardiovascular events and mortality.

Cost and Availability of ABPM

A number of authorities recommend ABPM as a cost-effective investigation, based mainly on the fact that the procedure identifies white-coat hypertension and prevents patients with a transient rise in BP from being prescribed BP-lowering drugs. The issue of cost-effectiveness of ABPM has been considered from a number of perspectives. First, ABPM may enable financial savings in drug prescribing by demonstrating the efficacy of antihypertensive drugs throughout the 24 hours. Adjustment of antihypertensive therapy according to ABPM rather than office BP has been shown to result in less antihypertensive medication being prescribed without compromising target-organ involvement. Second, by identifying patients with white-coat hypertension ABPM may improve drug prescribing in a cost-effective manner, and ABPM can also identify those subjects with normal BP in the office but elevated BP levels in daily life (masked hypertension), a condition that has been shown to carry the same adverse prognosis as sustained arterial hypertension both in the clinic and in daily life, and is therefore an indication for adequate pharmacological treatment.

Until recently ABPM has been generally cited as being more expensive than other measurement techniques; however, it has been shown that ABPM is cost-effective, both in specialist services and in primary care.33 The technique can achieve potential savings of 3% to 14% for cost of care for hypertension and 10% to 23% reduction in treatment days when ABPM was incorporated into the diagnostic process at an annual cost that would be <10% of treatment costs,34 and it is particularly cost-effective for the diagnosis and management of newly diagnosed hypertension.35 Recently, a detailed cost–benefit analysis was undertaken by NICE and showed that the use of ABPM is the most cost-effective method of confirming a diagnosis of hypertension in a population suspected of having high BP based on a conventional BP screening measurement >140/90 mm Hg and that the technique would result in substantial savings to the UK National Health Service.4,36 Other potential benefits of ABPM that have not been considered by NICE are the savings to be made in having drug treatment targeted to achieve 24-hour BP control and the substantial savings to be made by the prevention of stroke and other cardiovascular consequences of hypertension with improved BP control. NICE has not considered the potential benefits of identifying the white-coat and masked hypertension phenomena in treated subjects or of treating nocturnal hypertension, which is a major predictor of outcome. However, it should be mentioned that the validity of the underlying assumptions by NICE has not been universally accepted on the basis that the strength of evidence is always difficult to assess.37 However, the robust cost-effective analysis adopted by NICE has not been questioned and stands as the most comprehensive analysis of its kind.

Because the cost of ABPM and hypertension management differ greatly from country to country and is dependent on the method of healthcare delivery, the cost-effectiveness of ABPM may need to be evaluated at a national level. For example, in Japan, it has been estimated that the introduction of ABPM for the management of hypertension has reduced medical costs by ≈9.48 trillion yen during 10 years.38 The ready provision of ABPM in primary care is dependent on reimbursement to physicians or other healthcare providers by the national healthcare systems or by private insurance and varies considerably from country to country with many countries not providing any reimbursement.6

Who Should Perform ABPM?

Despite the large diversity in the structure of healthcare systems across different countries, the vast majority of patients with hypertension are being managed in primary care. Thus,
in practice, primary care doctors may establish their own ABPM service, or alternatively they may refer their patients to an external ABPM service, as they routinely do for multiple other medical tests. Models to develop such services are being currently tested in several countries and might include specialist clinics, healthcare providers in the private sector, pharmacy-based services, and other solutions.

Although primary care practices and hypertension centers will be the main providers of ABPM, the valuable role of pharmacies in achieving improved control of hypertension has been recognized for many years. Indeed it has been shown that when pharmacists become engaged in the management of hypertension, BP control improves, and therefore the pharmacy might be a very appropriate setting in which to initiate the wide referral of patients for ABPM in collaboration with primary care physicians and/or specialists. Recently, ABPM has been introduced to pharmacists in a few European countries, and the pharmacy-based service is proving popular with patients and is being increasingly adopted, as shown in a recent Irish report.

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Disclosures

E. O’Brien is the medical director, a member of the Board and a shareholder of Dabli Ltd, Ireland. All authors have assessed and validated blood pressure (BP) measuring devices for a number of BP manufacturing companies.

References

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