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Ambulatory Blood Pressure Measurement

The Case for Implementation in Primary Care

Eoin O'Brien

Since Riva-Rocci and Korotkoff gave us the technique of conventional blood pressure (BP) measurement over a century ago, we have landed men on the moon, encircled Mars, invented the automobile and airplane, and, most importantly, revolutionized the technology of science with the microchip. Why, we might ask, has medicine ignored scientific evidence for so long so as to perpetuate a grossly inaccurate measurement technique in both clinical practice and hypertension research? The same sentiment has been expressed by Floras: "As a society, we are willing to contemplate widespread genomic or proteomic subject characterization in pursuit of the concept of 'individualized medicine.' By contrast, blood pressure measurement is one of the few areas of medical practice where patients in the twenty-first century are assessed almost universally using a methodology developed in the nineteenth."[1]

It is generally accepted that traditional clinic or office BP measurement (OBPM) is limited in the amount of information that it can provide for the adequate management of hypertension and that contemporary practice must turn to out-of-office measurement to obtain additional information to guide the diagnosis and management of hypertension. The methods available for out-of-office measurement are ambulatory BP measurement (ABPM) and self- BP measurement (SBPM). The purpose of this review is not to restate the criteria for measurement by these techniques, which have been described in detail previously,[2,3] but rather to present evidence to support the opinion that ABPM should be available to all primary care physicians who are responsible for the management of the majority of patients with hypertension. Hypertension is a major global risk for cardiovascular morbidity and mortality,[4] and the World Health Organization, aware of the paucity of BP measurement devices in low-resource countries is piloting studies to redress this serious deficiency.[5] Clearly, therefore, the out-of-office techniques addressed in this review will be out of reach of most low-resource countries, which require novel approaches, and apply to primary care in the developed world.[6]

Out-of-Office BP Measurement

Out-of-office BP measurement is big business. The worldwide market for BP monitoring and measurement instruments was estimated to be US$ 1.56 billion in 2006 and is projected to reach $2.14 billion by 2010.[7] Many SBPM devices sold on the world market are not independently validated and may be inaccurate; despite repeated recommendations that SBPM should only be performed under medical supervision, the reality is that patients purchase devices assuming them to be accurate and then use them without medical direction.

There can be little argument about ABPM and SBPM being superior to OBPM, if for no other reason than being free of the white coat reaction that gives OBPM levels considerably higher than those measured away from the medical environment in as many as 20% of individuals with suspected hypertension and in most patients with hypertension.[8] There has been debate, however, as to whether SBPM or ABPM is the preferred out-of-office measurement. Rather than arguing for 1 technique over the other, both techniques, as with OBPM, give differing information about BP behavior (Table) that may assist in understanding and managing hypertension.

It is often wrongly assumed that SBPM can give an assessment of a patient's true BP approximating to daytime ABPM, whereas the reality is that, to obtain a BP profile that equates to ABPM, it is necessary to adhere to a comprehensive schedule of SBPM requiring the patient to perform SBPM over several days. Although there have been calls for limiting the number of SBPM readings in clinical practice,[9] there is general support for the recommendation of the European Society of Hypertension Working Party on Blood Pressure Monitoring[2] for daily duplicate morning and evening SBPM measurements on 7 days, with the first-day readings being discarded and the remaining measurements averaged.[10–12] From the convenience viewpoint, the 2 methodologies for providing out-of-office BP make distinctly different demands on the patient. To obtain meaningful SBPM, the patient must be prepared to make multiple measurements over 7 days, whereas with ABPM, the patient is required to have multiple measurements over 1 day, with the added advantage of the nocturnal BP being available for analysis.

Another fundamental difference between SBPM and ABPM is that the physician must trust patient compliance to the SBPM regimen, whereas with ABPM the physician

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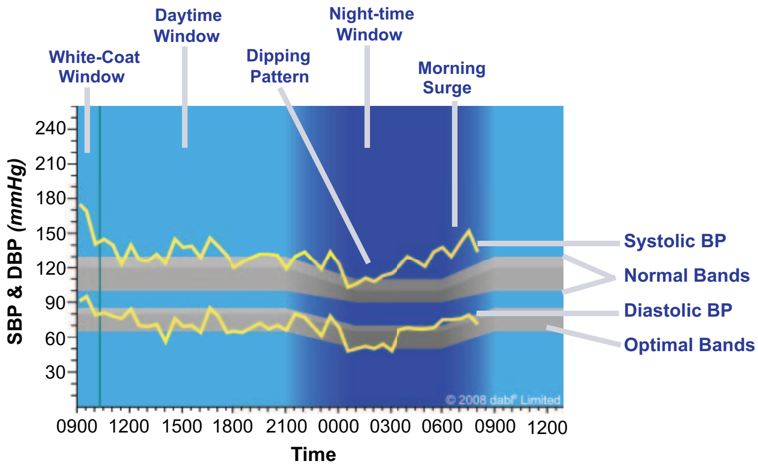

Automatic Interpretation

The ABPM suggests borderline 24-hour systolic hypertension (133 mmHg daytime, 118 mmHg night-time) and normal 24-hour diastolic blood pressure (71 mmHg daytime, 59 mmHg night-time) with a white-coat effect (175 mmHg/95 mmHg).

Statistical Analysis

	SBP	DBP	MAP	HR
White-Coat Window				
Readings	3	3	3	3
First hr max	175	95	124	50
Daytime (09:00-21:00)				
Readings	21	21	21	21
Mean	**133**	**71**	90	44
SD	8	7	8	3
Night-time (01:00-06:00)				
Readings	10	10	10	10
Mean	**118**	**59**	81	40
SD	9	8	10	2
24-hour				
Readings	43	43	43	43
Mean	129	68	88	42
SD	11	9	10	3
Dip %	11	17	10	8

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Figure. Example of a standardized interpretative ABPM report. The levels of normality are based on latest outcome-based thresholds, which give daytime ABPM values of 130/85 mm Hg and nighttime values of 110/70 mm Hg.[54] SBP indicates systolic BP; DBP, diastolic BP; MAP, mean arterial pressure; HR, heart rate; Dip, percentage dip in nocturnal BP.

controls the procedure, and the ≈50 BP measurements obtained over the 24-hour period are recorded and stored. Importantly, as will be seen from the Table, ABPM provides a wealth of information that cannot be derived from SBPM, and although much of these data may only be required for research, the provision of daytime and nighttime BP with ABPM is generally considered to make ABPM indispensable to good clinical practice.[1,2,12–14]

The use of ABPM and SBPM is recommended by several national and international guidelines for the management of hypertension in Europe and the United States.[2,15] The exclusion of white coat hypertension is accepted by most guidelines as being a definitive indication for ABPM, but in the absence of any clinical characteristics to indicate when white coat hypertension is present, it is difficult not to agree with the view expressed by the European Society of Hypertension that patients in whom a diagnosis of hypertension is being contemplated based on an elevated OBPM should have ABPM to exclude white coat hypertension.[16]

Can Electronic Transmission of Data Facilitate the Use of Out-of-Office BP in Primary Care?

The devices currently available for ABPM have been subjected to independent validation, mostly according to the European Society of Hypertension International Protocol, and are accurate. However, although SBPM devices have improved in this regard in recent years, a large number of unvalidated devices may be purchased by patients.[17] It is important for physicians and patients using either SBPM or ABPM to ensure that the device being used has been recommended for clinical use by checking the Web site (www.dableducational.org), which provides the latest accuracy data on all BP measuring devices.

There is now increasing interest in improving out-of-office BP by electronic transmission of data. One of the major disadvantages of early stand-alone SBPM devices was the need to enter measurements on record cards, which allowed BP measurements to be manipulated by patients. The introduction of devices for SBPM with the facility to automatically store data or print out results with the time and date of measurement has largely overcome this problem.[18] Telemonitoring of SBPM data has been a further improvement that gives the physician a supervising role in the patient's use of SBPM while also improving compliance to treatment and leading to improved BP control.[19,20] More recently, mobile telephone transmission of data from SBPM has been successfully initiated.[21] Teletransmission of SBPM data has also been used in pharmacological studies,[22] and, recently, adjustment of treatment by patients based on telemetric data has been reported.[23] Although patients with hypertension may welcome the sharing of care provided by telemetry, physicians may be wary of their increased accessibility to patients and the potential for increasing their workload without remunerative processes being in place.

Table. Qualities of and Information Provided by BP Measurement Techniques

Qualities of Measurement	OBPM	SBPM	ABPM
General features			
Cost	Inexpensive	More expensive than OBPM but cheaper than ABPM depending on complexity of devices and provision of telemetry	More expensive that OBPM or SBPM but cost-effective
Medical requirements	Conventional technique in clinical environment under medical supervision	Should be used under medical supervision, but device often purchased and used without medical supervision	Must be used and interpreted under medical supervision
Need for training	Doctors and nurses should be trained and tested for competence	Minimal medical training required, but patients should receive medical instruction	Training required, but software can facilitate process
Duration of procedure	Brief depending on No. of measurements recorded	To equate with daytime ABPM, BP should be measured ×2, morning and evening, for 7 days, with first day discarded and 24 BPs averaged	Usually 24-h BP measurements at 30-min intervals during day and night with minimal requirement of 14 daytime and 7 nighttime measurements
Validated accuracy (for accuracy of all devices see: www.dableducational.org)	Automated devices replacing mercury sphygmomanometers	Many devices on the market are not independently validated for accuracy	Most ABPM devices on the market have been validated independently for accuracy
Identification of hidden phenomena			
White-coat hypertension	OBPM ≥140/90 mm Hg	SBPM <135/85 mm Hg	Daytime ABPM <130/85 mm Hg* Most effective means of identifying white-coat hypertension
White-coat effect	OBPM higher than SBPM or ABPM	SBPM ≥135/85 mm Hg	Daytime ABPM >130/85 mm Hg*
Masked hypertension	OBPM <140/90 mm Hg	SBPM ≥135/85 mm Hg	Daytime ABPM >130/85 mm Hg* Most effective means of identifying masked hypertension
Siesta dipping	Cannot be diagnosed with OBPM	Difficult to diagnose with SBPM	Hypotension on ABPM during siesta
Nocturnal patterns: dipping and nondipping; reverse dipping; extreme dipping; morning surge; isolated nocturnal hypertension	Cannot be diagnosed with OBPM	Cannot be diagnosed with SBPM	Patterns apparent on ABPM
Identification of BP patterns			
Systodiastolic hypertension	Commonest diagnosis	Better assessment of severity	Allows assessment of severity over 24 h
Isolated systolic hypertension	SBP ≥140 and DBP <90 mm Hg	SBP ≥135 and DBP <85 mm Hg	SBP ≥130 and DBP <85 mm Hg* Allows diagnosis of day and/or nighttime ISH
Isolated diastolic hypertension	SBP <140 and DBP ≥90 mm Hg	SBP <135 and DBP ≥85 mm Hg	SBP <130 and DBP >85 mm Hg* Allows diagnosis of day and/or nighttime IDH
Prediction of outcome			
Target organ damage, cardiovascular morbidity, and mortality	Has been the measure of outcome in the past	Superior to OBPM	Superior to OBPM and SBPM
Provision of indices			Nocturnal hypertension may be sensitive predictor
24-h heart rate; 24-h mean BP; 24-h pulse pressure; measures of variability; ambulatory arterial stiffness index; cusum plots; cardiovascular load; area under the curve	Not applicable	Not applicable	Can be computed from ABPM recordings

(*Continued*)

Table. Continued

Qualities of Measurement	OBPM	SBPM	ABPM
Guide to drug prescribing			
Efficacy of treatment over time	Poor guide because of white-coat response and limited BPs	Moderate guide to daytime efficacy that can be readily repeated	Allows assessment of efficacy over 24-h period
Nocturnal BP control	Not applicable	Not applicable	Allows assessment of nocturnal lowering of BP
Reduction of morning surge	Not applicable	Not applicable	Allows assessment of treatment effect on morning surge
Detection of excessive BP lowering	Limited because of infrequency of measurement	Better than OBPM	Allows detection of hypotensive episodes throughout the 24-h period
To improve compliance to treatment	May have a minor influence	Major advantage of SBPM	Provision of ABPM record to patient can be helpful
To evaluate drug-resistant hypertension	Poor guide because of white-coat response and limited BPs	Provides better assessment than OBPM	Removes white-coat effect and shows if BP elevation is persistent
Identification of hypotensive patterns			
Postural hypotension	Difficult to diagnose with OBPM	Fall in standing SBPM	Time, duration, and relationship to hypotension can be documented
Postprandial hypotension	Difficult to diagnose with OBPM	Fall in SBPM after meals	Fall in ABPM after meals
Drug-induced hypotension	Difficult to diagnose with OBPM	Can be detected with SBPM after drug ingestion	Time, duration, and relationship to drug intake can be documented
Idiopathic hypotension	Difficult to diagnose with OBPM	Can be detected if SBPM related to hypotension	Best diagnosed with ABPM
Autonomic failure	Difficult to diagnose with OBPM	Not detectable because of lack of nighttime BP	Daytime hypotension and nocturnal hypertension

Many of the above features of ABPM are applicable also in pregnancy and become of even greater relevance in high-risk patients, such as those with diabetes and in the elderly, who may have complex patterns of 24-hour BP. Data are from References.[2,3,16,24] SBP indicates systolic BP; DBP, diastolic BP; ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension.

*These levels are based on latest outcome-based thresholds, which give daytime ABPM values 130/85 mm Hg[54] as compared with 135/85 mm Hg, recommended by the European Society of Hypertension.[2]

As with SBPM, developments in software and electronic transmission of data have been used to make the technique of ABPM more accessible to clinical practice. The dabl ABPM program generates a graphic presentation of ABPM data in a standardized format, demarcates the bands of normality, and provides a computer-generated interpretative report (Figure).[2,3,24,25] Because ABPM has been shown to significantly improve BP control in primary care,[26,27] advances have been made in central hosting and analysis of ABPM data. For example, the Spanish Society of Hypertension has developed a nationwide project to promote the use of ABPM in primary care settings based on central analysis of ABPM data transmitted electronically.[28]

Experience With ABPM in Primary Care

One of the first studies of ABPM in primary care showed that BP measurements made by doctors were much higher than those using ABPM, leading the authors to conclude that it was "time to stop using high BP readings documented by general practitioners to make treatment decisions."[29] Another study using ABPM in primary care showed that office BP incorrectly labeled nearly a third of patients with a white-coat effect as having poor BP control and that these patients were likely to be recalled for unnecessary follow-up and intervention.[30] An Irish study in primary care showed that only 12% of patients achieved target BP with OBPM 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 OBPM, who were candidates for drug treatment, were not commenced on medication because ABPM was normal.[26]

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 is being established.[27,28] In this large cohort of some 20 000 patients, clinic BPs were ≈16/9 mm Hg higher than ABPM in patients categorized as being at low-to-moderate added risk, with a greater difference (23/23 mm Hg) in those categorized as being at high risk in spite of receiving much more antihypertensive treatment. Moreover, high-risk hypertensive patients showed a high prevalence of circadian rhythm abnormalities on ABPM, with the prevalence of a nondipping pattern being ≈60%, and in patients with the lowest ABPM levels, high-risk patients showed a higher prevalence of nondipping nocturnal BP than lower-risk cases. An editorial commentary on this study urges the wider use of ABPM to gain more accurate risk categorization of patients in the community and to be able to obtain a more accurate estimate of the community control of BP.[31] As in the Irish study, BP control was better when assessed by

ABPM than by OBPM, indicating that the white-coat effect with OBPM is leading to an underestimation of BP control in the community.[26–28] BP control was underestimated in more than one third of patients and overestimated in some 5% by OBPM as compared to ABPM. Notably, BP was uncontrolled by both methods of measurement in 43% of patients. High-risk patients showed poorer ABPM control then low-to-moderate–risk patients in spite of receiving much more antihypertensive treatment.[27,28]

Savings in Drug Prescribing

White et al[32] have shown that ABPM in pharmacological trials in primary care provided excellent control rates for the antihypertensive drug being assessed and showed that the observer and measurement bias present on clinical measurement was absent with ABPM. The superiority of ABPM over OBPM in managing antihypertensive medication has been demonstrated in a number of clinical studies. Adjustment of antihypertensive therapy according to ABPM rather than OBPM has been shown to result in less antihypertensive medication being prescribed without compromising target organ involvement.[33] It has also been shown that, in patients on treatment with BP-lowering drugs, ABPM was a better predictor of cardiovascular outcome than OBPM.[34] Amelioration of the white-coat effect, especially in elderly patients, who have greater BP variability, may be attributed wrongly to a BP-lowering effect of antihypertensive medication if ABPM is not used to assess treatment efficacy.[35] The long-term cost of care for hypertension is dominated by costs for drug treatment, rather than for visits and investigations.[36,37] However, costs for the first year of management tend to be higher than for subsequent years, and the use of ABPM to reduce the cost of treatment will be most effective when implemented to detect white-coat hypertension and to improve drug prescribing in a cost-effective manner.[38]

ABPM is more expensive than OBPM, but the technique has been shown to be cost-effective, both in specialist services and in primary care.[38,39] Traditionally, the cost-effectiveness of ABPM has been considered in terms of the tangible benefits, such as identifying patients with white-coat hypertension, and the savings that might be made from the more efficient prescribing of BP-lowering drugs. However, cost-effective considerations must be extended to include the financial potential of the technique to improve not only the diagnosis and management of hypertension, but as a means of ensuring that effective control of hypertension is implemented at community level.

Identification of White-Coat Hypertension

ABPM is the most effective technique for identifying white-coat hypertension, which may be present in as many as 20% of people who appear to have hypertension with OBPM, and these patients may be spared years of unnecessary and expensive drug treatment, as well as avoiding being penalized unnecessarily for insurance or employment by having the diagnosis of "hypertension" misapplied. White-coat hypertension is the only indication approved by the Centers for Medicare and Medicaid Services in the United States.[16] The most recent and thorough cost benefit analysis by Krakoff showed that 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.[38] Put another way, these cost-benefit analyses show that ABPM is cost-effective for the diagnosis and management of newly diagnosed hypertension.[39]

Identification of Masked Hypertension

Masked hypertension is the reverse of white-coat hypertension in that patients have normal OBPM but elevated daytime ABPM. The prevalence of masked hypertension seems to vary between 10% and 20%, but even if the prevalence was only 5%, this number applies to the whole adult population, not just the proportion of the population with hypertension, which translates into ≈10 million people in the United States.[40] SBPM may also detect masked hypertension, but whether similar patients will be detected by both ABPM and SBPM remains to be seen.[41] Indeed, it is a salutary thought that if white-coat hypertension is present in 20% and masked hypertension in 10% of the population when BP is measured conventionally in primary care, it follows that the diagnosis of hypertension is being misdiagnosed in as many as one third of all patients attending for routine BP measurement.[42]

The importance of masked hypertension as a clinical entity rests on the fact that those with the condition are not only at increased risk of developing sustained hypertension, but they also have increased target organ involvement as denoted by left ventricular mass and carotid atherosclerosis and, as might be expected when target organ involvement is increased, they also have increased cardiovascular morbidity. The logical extension of this line of reasoning is that future studies will also show cardiovascular mortality to be increased.[43,44] Masked hypertension presents clinicians with the serious problem of identifying subjects with the condition. Clearly, it is not practical to perform ABPM in all subjects with normotension in the office or clinic to unmask those with ambulatory hypertension. Yet, the consequences of not identifying masked hypertension carry serious implications for patients who may already have overt coronary and cerebrovascular disease in whom BP-lowering medication would be the single most important therapy in preventing recurrent stroke or heart attack. The best policy for the moment would seem to be to perform ABPM in patients with high-normal OBPM who are at high risk of developing cardiovascular disease due the presence of multiple risk factors and in patients with associated morbidity, such as diabetes mellitus, a previous history of a cardiovascular event, or those with evidence of target organ damage.

Identification of Nocturnal Hypertension

Nighttime BP measured by ABPM is superior to OBPM in predicting cardiovascular events.[13,14] In the Spanish study in primary care, the prevalence of a nondipping BP pattern was ≈60%, and this was more likely in high-risk patients.[27,28] The importance of measuring BP over the 24-hour period has been stressed in the recent International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes analysis in 7458 people, which showed that both daytime and nighttime BP contribute differing information on outcome, which may be influenced by antihypertensive medication.[14] Recent studies have drawn attention to the importance of controlling not only daytime but also nighttime BP.[45,46] In this regard, control of the early morning surge may prove to be particularly important in preventing stroke.[47] It follows, therefore, that if nocturnal BP control, which can only be assessed with ABPM, is important in preventing cardiovascular events, ABPM should be available to ensure that 24-hour BP control is achieved in hypertensive patients.

Conclusion

Individuals over age 60 years represent the most rapidly growing segment of the US population, with the average life expectancy of people born in the United States in 2003 being 77.6 years.[48] Projections for the European region suggest that the proportion of the population aged ≥65 years will increase from 20% in 2000% to 35% in 2050, and the median age will rise from 37.7 years in 2000 to 47.7 years in 2050.[49] The prevalence of hypertension increases with advancing age to the point where more than half of people aged 60 to 69 years old and approximately three fourths of those aged ≥70 years are hypertensive.[15] Because the predominant determinants of stroke are hypertension and age, it is hardly surprising that increased age carries an increased risk of stroke and that with increasing longevity the incidence of stroke is rising; eg, in Europe, stroke rates increased from ≈5000 per 100 000 in subjects aged <75 years to ≥10 000 per 100 000 in those aged >80 years.[50]

Improved BP control could have a major impact on these daunting statistics. For example, a meta-analysis of 8 placebo-controlled trials in 15 693 elderly patients followed for 4 years showed that active antihypertensive treatment reduced coronary events (23%), strokes (30%), cardiovascular deaths (18%), and total deaths (13%), with the benefit being greatest in patients >70 years of age.[51] Hypertensive patients in whom BP is uncontrolled by treatment have a cardiovascular risk only modestly less than that of untreated individuals,[52] which leads to the conclusion that, in practice, BP-lowering drugs are prescribed inappropriately without achieving optimal control, or, put another way, "patients are frequently not barely but badly controlled."[12] This therapeutic inertia, whereby the prescribing of medication is seen as constituting an end in itself in that some good will be achieved, must now be replaced by a clinical modus operandi, recognizing that the efficacy of medication will ultimately determine the fate of the patient with hypertension.[53] Efficacy, however, can only be gauged by the achievement of evidence-based target levels of BP, which, in turn, demands accurate BP measurement that should also be capable of indicating BP control over the 24-hour period.

Given these facts, it seems that there should be an imperative to change contemporary clinical practice if we are to avert the burden of stroke and heart failure in an aged population. We have adequate drugs to achieve effective BP lowering in the vast majority of patients; what we lack is the determination to achieve effective BP control as early as possible. In light of the evidence available on the societal and financial consequences of uncontrolled hypertension, we must no longer quibble over the cost of technology to measure BP. Every patient suspected of having hypertension should have ABPM to confirm or refute the diagnosis, and every patient with uncontrolled hypertension should have ABPM repeated as necessary until 24-hour control of BP is achieved.

Disclosures

The author has contributed financially to the development of the dablR ABPM software program and is a member of the Board of dabl Limited (www.dabl.ie).

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