CONTROVERSIES IN HYPERTENSION

Ambulatory Blood Pressure Monitoring Is Ready to Replace Clinic Blood Pressure in the Diagnosis of Hypertension

Pro Side of the Argument

Geoffrey A. Head

Since the introduction of lightweight ambulatory blood pressure (BP) monitoring (ABPM) devices into clinical use in the late 1980s, there has been a huge increase in their contribution not only to fundamental research on the diurnal patterns of BP in humans, but increasingly for the diagnosis of hypertension. Clearly, the recognition of the value of multiple readings for accuracy and the detection of white coat, masked, and nocturnal hypertension has been critical to correctly determine the extent and impact of hypertension in the community. Importantly, the prognostic value of ABPM for cardiovascular events has been a major impetus for the promotion of its widespread adoption in primary care. National and International guidelines have largely been supportive of this move, and the United Kingdom leads the way by adopting ABPM to diagnose hypertension in primary care. Thus, the question of whether ABPM is ready to replace clinic measurements for the diagnosis of hypertension is passé for some but still relevant for others. In either case, the arguments for and against need to be carefully considered as there are major implications to the way cardiovascular healthcare services are delivered. The case for using ABPM for the diagnosis is strong given that clinic measurements even when performed to best practice standards misdiagnose hypertension in ≈30% of individuals (see below). The evidence is so convincing that the medico-legal issue of NOT performing ABPM to diagnose hypertension has been raised. On the contrary, there is resistance to using ABPM particularly in some quarters exemplified by the editorial in 2011 that suggested that ABPM is not ready for prime time. The arguments presented are largely related to resources and costs and suggested alternatives.

In order therefore to consider this important question, we need to first evaluate the medical imperative for the use of ABPM over other alternatives to determine whether they match the diagnostic sensitivity of ABPM. Second, we need to determine whether the barriers of implementation really exist or whether they are simply inertia to change. It is understandable that the office/clinic measurement of BP has been the cornerstone of clinical screening for hypertension, but is also used for a myriad of other reasons in assessing patient’s health and condition. This should continue and be improved with wider use of automated office BP devices. However, the proper diagnosis of hypertension requires a much more accurate assessment of the patient’s BP during their normal active life, during the night, and importantly, during the sleeping period, which is afforded only by ABPM. Although the current brief is to support the case that ABPM is ready to replace clinic BP in the diagnosis of hypertension, it is not to discuss the growing support for the use of ABPM in guiding drug treatment or 24-hour efficacy of drug treatment, which is a separate but still important issue.

ABPM Is the Most Accurate Method for Diagnosis

Of the 3 most common modalities for the assessment of BP, clinic, home, and ambulatory, the latter has been well recognized to best reflect the individual’s BP profile over the 24-hour period. Current estimates from 3 studies suggest that clinic
BP assessments misdiagnose hypertension in 9%,6 12%,7 and 18%5 of the general population where the measurements are sufficiently above the hypertension threshold of 140/90 mmHg in the office but below threshold outside the office. This phenomenon was defined by Pickering and colleagues as White Coat or isolated clinic hypertension4 and is thought to be largely because of the stress of the occasion.9 Conversely, a further =10% are misdiagnosed by clinic measurements when the patient’s BP levels are below the hypertension threshold in the office but are above outside the office.10,11 This is termed masked hypertension.12 Thus, taken together, misdiagnosis can occur in 20% to 30% of patients if classified with clinic assessments.

The Prognostic Value of Ambulatory BP Monitoring

One of the strongest arguments for the use of ABPM over clinic BP has come from its greater prognostic value. This presumably derives from the sheer number of recordings, likely giving a more reliable measure of the patient’s real BP. Further, the 24-hour assessments include multiple measurements during the normal person’s daily schedule, measurements at night reflecting the importance of BP dipping. Thus, it is not at all surprising that so many prospective studies have found that ABPM measurements are a much stronger predictor of clinical outcomes than clinic BP assessments.31–30 End-organ damage associated with elevated BP, such as left ventricular hypertrophy, is more strongly correlated with ABP than with clinic BP measurements.31–34 ABPM also correlates more closely with renal and vascular surrogate markers of end-organ damage, such as microalbuminuria and carotid artery wall thickness, respectively.35 Of the ABPM measures, night time BP is a stronger predictor of end-organ damage than daytime BP.29 The well-accepted underlying argument is that the end organ damage is a surrogate for the long-term level of BP of the individual patient. Since ABPM is clearly ahead of other BP measure in this regard, it likely better reflects the true BP of the patient.

The inaccuracies of clinic measurements are well described, but in the main they are caused by the relatively few measurements taken under often less than optimal conditions. Further, neither clinic nor home BP assessments include nocturnal BP. There have been few direct comparisons between clinic, home, and ABPM as to which is the best predictor of outcome. The study Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) found that both home and ABPM were similar in their prognostic ability, but this study was limited in that no cofounders were adjusted for, cardiovascular mortality was the only end point, and home measurement consisted of only 2 readings.29 Further, the predictive capacity of the 3 methods was based on only 56 end points, too few to be meaningful. Recently, Niiranen et al26 directly compared the prognostic value of ABPM and Clinic BP in predicting cardiovascular mortality, myocardial infarction, stroke, heart failure hospitalization, and coronary intervention in 502 participants followed up for 16 years. When all BP measures were included in the multivariate adjusted Cox models, only systolic and diastolic ambulatory BP was a predictor, indicating the ABPM is superior to office measurements.26 Importantly, the office BP was meticulously determined by a nurse after 15 minutes rest using 4 duplicate measures at weekly intervals.

What Do the Guidelines Say?

In the last 5 years, several guideline updates have included ABPM and have made much stronger recommendations for its use. In particular, The National Institute of Clinical Excellence in the United Kingdom in 2011 stated “If the clinic BP is 140/90 mmHg or higher, offer ABPM to confirm the diagnosis of hypertension.”37 This recommendation was the result of an exhaustive systematic review of the literature (over 600 papers) and grading of the evidence which is presented in table form. Although only a selection of these papers referred to the issue of measurement of BP, the analysis of primary papers and many meta-analyses provided clear evidence that although home BP assessments were superior to clinic measurements for the diagnosis of hypertension, they were not as good as ABPM.35 The Australian ABPM consensus statement recommended clinic blood for screening and a combination of ambulatory, home, and clinic measurements for diagnosis of hypertension.38 More recently, the European Society of Hypertension working group on BP monitoring released a most comprehensive position statement9 and also a practice document.40 The European Society of Hypertension working group strongly 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. In Japan, the 2012 revised guidelines for the use of ABPM suggests that the procedure should not be used as a routine procedure, but was an excellent tool for detailed evaluation of BP during normal daily life. The committee suggested it should be used only for those with large variability of BP or suspected white coat, masked, or resistant hypertension.41 In reality, how does one suspect white coat hypertension without the use of ABPM or other out of office techniques. As in the United States, ABPM has been reimbursed in the Japanese National Health Insurance scheme, which recognized the superiority of ABPM over casual BP measurements for predicting the development of cerebral and cardiovascular complications.41

The approach of the Canadian Hypertension Education Program recommendation for management of hypertension published in 2010, which is still current, follows a logical algorithm of ≥2 office visits with BP elevated above the standard hypertension threshold (140/90mmHg) to be confirmed for diagnosis by either (i) 3 further office visits with average values above threshold, (ii) an ABPM, or (iii) home BP measurements. Thus, although there is a degree of flexibility in which BP technique can be used for the diagnosis of hypertension in the Canadian recommendations, there is a clear support for ABPM and home measurements, which are recommended with higher level of evidence (Grade C) compared with clinic measurements (grade D). Inherent in the guidance is recognition of the poor reproducibility of clinic measurements requiring 5 clinic visits to confirm diagnosis of grade 1 hypertension compared with a single ABPM.

Guidelines tend to be conservative by nature, but most panels are clearly recognizing the issues related to the inaccuracy of clinic BP and the value of ABPM not only in special cases.
but more generally for the most accurate assessment of the patients' BP but also for the diagnosis of hypertension. The National Institute of Clinical Excellence (UK) recommendation provides the most thorough analysis of the issue, and although the recommendation was controversial,\textsuperscript{42} the advice is hard to refute given the extent of the evidence presented.

**Are There Hypertension Definitions and Thresholds for ABPM?**

A prerequisite for the readiness of using ABPM to replace clinic BP for the diagnosis of hypertension is the need for a comprehensive set of thresholds to define hypertension and guide treatment in both low and high risk patients. These are well documented for clinic BP and are in the main similar across the various national guidelines (see Table 6 in James et al.).\textsuperscript{43} These are now available for ABPM\textsuperscript{46} as well after a study that used a regression technique based on paired clinic and ABPM readings from over 5000 patients to determine ABPM equivalents (Table 1).\textsuperscript{44} The level of these thresholds based on the Australian National Heart Foundation guideline\textsuperscript{45} was partly validated by the finding that the method predicted exactly the internationally accepted levels of daytime, night time, and 24 hour ABPM equivalents for the hypertension threshold of 140/90 (Table 2).\textsuperscript{37,39,40,42} Further they closely matched the values determined by the International Database on Ambulatory BP and Cardiovascular Outcomes study, which used an outcome measure equivalent to determine the ABPM threshold for hypertension.\textsuperscript{46} Thus, a clear and valid framework for using ABPM in the diagnosis and treatment of hypertension in low and high risk patients is now available.

**Do Barriers to Using ABPM Really Exist?**

The influence that ABPM has on clinical practice clearly varies from country to country depending on ease of availability, cost, patient engagement, and importantly, the attitude of treating physicians. However, there has been some resistance to the concept of using ABPM to replace clinic BP. An editorial that responded to the publication of the National Institute of Clinical Excellence (UK) guideline in 2011 suggested that ABPM was not ready for prime time in the United States.\textsuperscript{3} The reason was given that without appropriate reimbursement from third-party payers in the United States, the equipment, staffing, and training costs to implement a similar recommendation for ABPM would be overwhelming. A similar message was reported by a spokesperson from The Royal Australian College of General Practitioners who were supportive of ABPM, but they were not pushing for a medical rebate because of costs and practical issues, such as training staff, and that home monitoring was simpler.\textsuperscript{40} The question of whether these barriers are real or not is therefore of decisive importance.

**Advances in ABPM Technology, Availability of Suitable Devices and Training**

Novel technological developments, including cloud based remote monitoring, integration into clinic patient management software, and new low patient impact devices that exist today, have removed many of the major barriers to the routine use of ABPM for diagnosis and management of hypertension. There are now a large number of smaller and lighter ambulatory devices, with some giving 24 hour measurement of central systolic, diastolic, and pulse pressure. According to the Medicalexpo web site, there are 30 companies offering 44 products for ambulatory BP. Nearly all have passed one of the accreditation schemes such as Association for the Advancement of Medical Instrumentation, British Hypertension Society, and European Society of Hypertension testing regimes. Some models offer dual cuffs for first visit screening. The integration and use of standardized analysis by easy-to-use software offers doctors an instant guide to the interpretation. Most software offers the standard measures of 24 hour, day night, awake, and asleep summary data, whereas some include circadian analysis, options for actigraphy to detect sleep, as well as online upload and analysis. Alternatively, detailed simplified guide to the use of standardized report information, as well as examples and interpretation, are available from the Australian ABPM consensus Committee\textsuperscript{46} as well as from the European

### Table 1. Classification of Hypertension and Treatment Targets for Adults According to Clinic Blood Pressure\textsuperscript{46} Mathematically Derived From the Relationship Between Clinic and ABPM\textsuperscript{38}

<table>
<thead>
<tr>
<th>Hypertension Thresholds</th>
<th>Clinic BP (mm Hg)</th>
<th>ABP Predicted From Clinic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24-h (mm Hg)</td>
<td>Night (mm Hg)</td>
</tr>
<tr>
<td>Grade 3 (severe)</td>
<td>180/110</td>
<td>165/100</td>
</tr>
<tr>
<td>Grade 2 (moderate; JNC7 Stage 2)\textsuperscript{43}</td>
<td>160/100</td>
<td>150/90</td>
</tr>
<tr>
<td>Grade 1 (mild/uncomplicated hypertension; JNC7 Stage 1)\textsuperscript{46}</td>
<td>140/90</td>
<td>130/80</td>
</tr>
<tr>
<td>Patients with associated clinical conditions or end-organ damage\textsuperscript{†}</td>
<td>130/80</td>
<td>125/75</td>
</tr>
<tr>
<td>Hypertension plus proteinuria &gt;1 g/d</td>
<td>125/75</td>
<td>120/70</td>
</tr>
</tbody>
</table>

Hypertension thresholds and targets are based on the National Heart Foundation of Australia definition\textsuperscript{44} and were equivalent for JNC7.\textsuperscript{45} Predicted mean systolic/diastolic ABP values rounded to the nearest 5 mm Hg corresponding to specific clinic BP levels and targets (upper limits) that are used in grading hypertension based on clinic BP measured by trained staff other than doctors.\textsuperscript{44} ABP indicates ambulatory blood pressure; ABPM, ambulatory blood pressure monitoring; BP, blood pressure; and JNC7, Seventh Joint National Committee.

*People without any of the following: coronary heart disease, diabetes mellitus, chronic kidney disease, proteinuria (>300 mg/d), stroke, or transient ischemic attack.

†People without any conditions listed at note [\textsuperscript{†}].
Society of Hypertension. Cloud-based centralized storage from blue tooth devices connected to smartphones also simplifies the uploading of the 24 hour profile, taking the hassle out of retrieving the data from the patient. As for training, this is no different and could be suggested as actually being easier than training staff to measure by traditional methods of BP measurement. It is clear that technology has and will continue to remove what can now only be conceived as a perception of a barrier rather than perhaps a real concern.

The availability of ABPM varies considerably between different countries and is perhaps one of the major barriers to implementing ABPM for the diagnosis of hypertension. A large study emanating from Ireland has recently examined the results of ABPM from over 46,000 patients attending primary care and nearly 1,700 patients with ABPM organized through pharmacies. The values obtained were within 1 mmHg and generally in good agreement with a similar percentage of white coat hypertension, although more people attending pharmacies were hypertensive. Nevertheless, the overall BP characteristics were similar. Thus, performing ABPM in Pharmacies is feasible and provides a useful adjunct to make ABPM much more accessible. Further, this study is an excellent example of the use of advanced centralized computer technology such as dabl for the collection, analysis, and dissemination of ABPM recording information, thus, reducing the burden on doctor’s and clinic staff time and empowering the patient in the management of their hypertension.

Cost-Benefit of Using ABPM for the Diagnosis of Hypertension

Formal cost-benefit analysis has consistently shown that ABPM reduces costs. In Japan, it was estimated that introduction of ABPM for hypertension would result in a saving of 10 trillion yen over 10 years, saving nearly 10,000 lives and reducing strokes by nearly 60,000. Positive steps in the United Kingdom and Europe are encouraging, including the 2011 modeling study on the cost effectiveness of 3 methods of primary care diagnosis of hypertension, which indicated robust cost savings for ABPM. Lovibond and colleagues suggested that ABPM would reduce misdiagnosis, reduce costs, and any additional costs from ambulatory monitoring are counterbalanced by cost savings from better targeted treatment. In primary care in Portugal, widespread use of ABPM for patients with suspected hypertension increases the diagnostic accuracy and improves cardiovascular risk stratification. Importantly, ABPM use reduces health costs, showing a highly favorable benefit–cost ratio compared with a strategy without ABPM. For the United States, Krakoff estimated a cost saving of 3% to 14% for cost of care for hypertension using ABPM for newly detected hypertensive subjects. Importantly, there were savings when the total annual cost of care was as little as $300. Similarly in Australia, a small but thorough study showed an overall 13% cost reduction to the pharmaceutical benefits scheme over 7 years and that the cost of ABPM was offset in the first year by less unnecessary treatment. A recent study suggests that there may be additional savings by using a chronic therapy approach, which is enabled by ABPM, for better control of daytime and nighttime BP levels.

Cost of Using ABPM for the Clinic and Patient

Competition has driven costs of devices down considerably and now some device manufacturers are even offering pay-per-use contracts, so there is no initial outlay at all. Reimbursement for ABPM has been considered to be an important issue holding back the implementation of ABPM for routine use. In the United States from 2001, ABPM could be claimed under Medicare for suspected white coat hypertensive patients. As in the United States, ABPM has been reimbursed by the Japanese National Health Insurance scheme, which recognized the superiority of ABPM over casual BP measurements for predicting the development of cerebral and cardiovascular complications as well as its excellent cost effectiveness. Further, in the only head-to-head comparison to guide determining antihypertensive treatment, ABPM guided therapy results in overall reduced prescriptions as clinic BP, while maintaining equal BP control and being as effective in reducing end-organ damage. In Australia, there is no rebate for ABPM, but advertised costs even in regional centers in Victoria are advertised as low as $40 for ABPM and $20 for concession holders. This equates to the cost to the patient of 1 month of a subsidized single antihypertensive agent.

For the clinic, cost recovery is a critical issue, and in the United States, in particular, the average cost of ABPM is considered to be high, but so are additional consultations that

<table>
<thead>
<tr>
<th>National Guideline</th>
<th>Clinic BP</th>
<th>ABP Equivalents, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seventh Joint National Committee (USA, 2003)</td>
<td>140/90</td>
<td>Not stated</td>
</tr>
<tr>
<td>European Society of Hypertension (2013)</td>
<td>140/90</td>
<td>130/80</td>
</tr>
<tr>
<td>Canadian Hypertension Society (1999)</td>
<td>140/90</td>
<td>130/80</td>
</tr>
<tr>
<td>Australian National Heart Foundation and High BP Research Council Consensus (2012)</td>
<td>140/90</td>
<td>130/80</td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence (UK, 2011)</td>
<td>140/90</td>
<td>Not stated</td>
</tr>
</tbody>
</table>

All values in mmHg. Note that the only discrepancy is for night time diastolic BP. ABP indicates ambulatory blood pressure; and BP, blood pressure.
would be required to properly confirm diagnosis. The current debate is often fixated on what we have always done in the past, and the power to make change through opening new markets and increased competition is not often considered. Not only are costs diminishing through technology, the proclamation of using ABPM for the routine diagnosis of hypertension will drive up the availability and drive down the costs. To use the argument that we are not ready to do this because the costs are too high or the tests are not easily available is not one that would be considered at all valid by innovators, such as Thomas Edison or Henry Ford. By creating the demand, you create the solution. The cost benefit analysis has already been done.

From the patient’s perspective, there is no doubt that faced with a choice of lifetime antihypertensive drug treatment or confirmation by a 24-hour ABPM test, the latter would be preferable, particularly for white coat hypertensive. This does not mean that they will always be able to remain treatment free as these patients eventually develop true hypertension in 1 to 2 years.

Are There Realistic Alternatives?

Automated Office BP

The final question to consider is whether there are realistic alternatives that make ABPM unnecessary. One such technique is automated office BP measurements that have been shown to increase accuracy, reduce the white coat effect, and give values equivalent of daytime ABP.65,66 Indeed, it has also been suggested that automated office BP is as good as home BP for assessing morning hypertension.67 However, a recent head-to-head comparison failed to show that automated office BP measurement improved classification errors compared with manual methods, although some lessening of the white coat effect was observed.68

Home or Self-Measurement of BP

Although the measurement of BP at home by the patient is an attractive option,69 there are considerations. For the diagnosis of hypertension, the patient is required to follow a demanding routine of measure twice in the morning and twice in the evening for 7 days, discarding the first day to gain an average of 12 readings.55 Importantly, home BP does not determine nocturnal BP, which is known to be the strongest predictor of outcome. The panel evaluating ABPM for Medicare in the United States stated It is important to note that self-measurement of home BP is not considered as a true alternative to ABPM.63 Home BP measurement can underestimate white coat hypertension and overestimate masked hypertension if the cuff size is wrong (normal instead of large) in patients with large arms.70 In terms of time and effort by the clinician, the training of staff to train the patient, gather the data, and interpret the findings exists for home BP assessment and is not too dissimilar to what is required for ABPM. Of concern is the quality of the readings, the patient bias, and the issue of the self–test induced effect (parallel to the white coat effect in the evening and morning for a week were 8/9 mm Hg less than daytime ABP, which suggest that home measurements did not accurately reflect normal daily life levels of BP. Thus, home BP has its place in conjunction with ABPM, but it should not be considered as an alternative unless ABPM is not tolerated. This is the current position of several guidelines, including those in the United Kingdom and Australia.37,38

Conclusions

After consideration of the issues, it is clear that there is compelling evidence to support the use of ABPM for the diagnosis of hypertension. Indeed, there would be concern from patient’s perspective if there was not a careful and accurate assessment of BP using the gold standard noninvasive method, before embarking, or not as the case may be, with antihypertensive therapy. Indeed, the medico-legal issue of not providing ABPM to patient’s in the light of the overwhelming recommendations for the use of ABPM to diagnose hypertension as raised recently by O’Brien2 may prove to be the final tipping point. The procedure is no more arduous than many others currently in use today for diagnosis of various conditions. The alternatives are not robust enough as yet, nor is the cost of ABPM a valid dissuader for its use. Are we ready now? Indeed, but the readiness does differ from country to country. The United Kingdom has already adopted the change to confirming diagnosis with ABPM into general practice. Given the importance of the outcome for the long-term health of the patient, other countries and regions should be encouraged to follow their lead sooner rather than later. The technological advances, competitive market, pay per use contracts have taken much of the difficulty and cost from the argument for many countries. However, realistically, in the developing world, it may not be affordable or practical at the moment.

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Disclosures

None.

References


Response to Ambulatory Blood Pressure Monitoring Is Ready to Replace Clinic Blood Pressure in the Diagnosis of Hypertension: Pro Side of the Argument

Josep Redon, Empar Larbe

The case for replacing clinic measurement of blood pressure (BP) with ambulatory blood pressure monitoring (ABPM) is based on the assumption that ABPM is the most accurate and cost-effective method to diagnose hypertension and assess the risk of hypertension-induced events. Moreover, a large number of reports and recommendations from Scientific Societies and Governmental bodies support this concept. However, before accepting these paradigms, the threshold values and the effect of BP-guided treatment on events should be determined. Threshold values for ABPM have been currently established by regression techniques and not from studies conducted to determine the BP values above which detection and treatment do more good than harm. Likewise, the optimal goals for antihypertensive treatment have not been established. In fact, though there are many studies comparing the effect of treatment on office BP and ABPM, evidence that ambulatory BP-guided treatment reduces morbidity and mortality is still required. Even though there is a large amount of experience and evidence supporting the superiority of ambulatory over office BP in the past years, its full effect remains to be tested over the coming years before the technique can be recommended as a replacement for office BP in the diagnosis and management of hypertension.
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对“动态血压监测在高血压的诊断中将替代诊室血压测量：辩论反方”的回应

Geoffrey A. Head

动态血压监测 (ABPM) 相对于诊室血压的优势是毋庸置疑的，在辩论中得到两篇文章的承认。反方指出，预后研究只是获得了研究开始时的测量数据，确实是这样，但是，在头对头比较的研究中这并没有实际意义 (反对理由1)。ABPM的价值不仅体现在多次测量具有更高的准确性上，而且还纳入了夜间血压，这在诊室内是无法做到的。确实，近期Niiranen等[1]的一项研究发现，诊室血压或家庭测量血压均达不到APBM的预后价值，这真正终结了这场特殊的辩论。所谓ABPM相关参数的局限性在这场辩论中没有意义（反对理由2）。对患者分类的不确定性 (反对理由3) 事实上在于诊室血压不能正确地诊断相当大比例的人群。这在很大程度上可以被ABPM消除。对于根据ABPM来定义高血压，目前已经有广泛的一致 (反对理由4)，如辩论正方所列的表1和表2，依据与诊室血压相当的原则[2]，确定了高血压的这些定义，并且在大型预后研究中得到验证[3]。采用ABPM指导治疗有明确的获益，已在这两篇文章中得到了概括性说明，治疗费用降低。这不是消极的 (反对理由4)。更加全面的成本获益分析现在明确支持ABPM。最后，ABPM的应用率 (反对理由5) 在快速提高，费用在不断下降，而且由于技术进步，需要的培训也在减少。鉴于支持ABPM的压倒性证据，我们甚至认为现在不推荐用ABPM诊断和管理高血压是一种失职的表现。

参考文献

Ambulatory Blood Pressure Monitoring Is Ready to Replace Clinic Blood Pressure in the Diagnosis of Hypertension

Geoffrey A. Head
冯颖青 审校

Since the 20th century, there has been a trend towards using ambulatory blood pressure monitoring (ABPM) to assess blood pressure in patients outside of a clinic setting. This method has been shown to provide more accurate and representative measures of blood pressure compared to traditional clinic-based methods. ABPM is particularly useful for diagnosing and managing hypertension, as it captures blood pressure throughout the day and night, providing a comprehensive view of blood pressure variability.

ABPM is most accurate in the diagnosis of hypertension, as it can identify individuals with white coat hypertension or masked hypertension, which may not be detected by traditional clinic measurements. It is also useful for monitoring responses to antihypertensive medications and for detecting hypertension in patients with a high risk of cardiovascular disease.

In conclusion, ABPM is an essential tool for the comprehensive assessment and management of hypertension. Its adoption in clinical practice has led to improved outcomes for patients with hypertension, and it is expected to continue playing a crucial role in the diagnosis and care of patients with this common and often asymptomatic condition.
动态血压监测的预后价值

有关ABPM优于诊室血压的最强论点之一来自于其较高的预后价值。这主要是由于记录的绝对数字更多，认为能更可靠地测量患者的真实血压。另外，24小时评估包括多次测量患者在正常日常活动中的血压值，测量夜间血压能够反映血压下降的重要性。因此，毫不奇怪，如此众多的前瞻性研究发现，与诊室血压测量相比，ABP测量是更强的临床预后因素[13,30]。终末靶器官损害与血压升高密切有关，如左心室肥厚与ABP的相关性显著于诊室血压测量[13-14]。ABPM与终末靶器官损害的肾脏及血管替代指标之间的关系更为密切，如微量白蛋白尿和颈动脉壁厚度[33]。在ABPM的测量数值中，夜间血压对终末靶器官损害的预测作用显著于白天血压[32]。普遍认为的理由是，终末靶器官损害是患者心血管疾病的一个重要指标。很明显ABPM在这种情况下优于其他血压测量方法，所以ABPM更可能反映出患者的真实血压水平。

诊室血压测量不准确的问题已经得到很好地说明，但是，他们基本上是由于测量次数相对较少引起，测量次数通常少于最佳情况。另外，诊室血压或家庭血压评估均不包括夜间血压。目前很少有研究直接比较诊室血压、家庭血压和ABPM，哪一种血压测量才是预后的最佳预测指标。Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) 研究发现，家庭血压和ABPM的预后能力相当，但是，该研究具有某些局限性，例如没有校正易感因素，心血管死亡率是唯一的终点，家庭血压测量只包含两个读数[33]。此外，这种方法的预测能力仅仅基于56个终点，终点事件太少，没有意义。最近，Niiranen等[34]对502例患者随访16年，直接比较了ABPM和诊室血压对预测心血管死亡、心肌梗死、卒中、心力衰竭住院和冠脉介入的预后价值。将所有的血压测量纳入校正后的多变量Cox模型中，只有动态收缩压和舒张压是预测指标，这提示，ABPM优于诊室血压测量[33]。更重要的是，诊室血压由一位护士在患者休息15分钟后仔细测得，重复测量4次，每隔一周测量。

指南如何说？

在过去15年中，多个指南更新将ABPM纳入其中，对于使用的推荐级别更强。特别是，英国的全国临床优化研究所（National Institute of Clinical Excellence）在2011年称，“如果诊室血压为140/90 mm Hg或更高，则采用ABPM以证实高血压的诊断[17]。”这一推荐是在对文献进行详尽地系统回顾（超过600篇论文）并且以表格的形式将证据分级之后作出的。尽管在有关血压测量的问题上，在这些论文中只有一个选择，但是，主要论文分析和许多荟萃分析提供了明确的证据，即尽管家庭血压评估在诊断高血压方面优于诊室血压测量，但是，家庭血压评估与ABPM并不是一样准确[37]。澳大利亚ABPM共识文件推荐，采用诊室血压筛查高血压，采用动态血压、家庭血压和诊室血压测量相结合的方法确诊高血压[38]。更近一些，欧洲高血压协会（European Society of Hypertension）血压监测工作组发布了一份最全面的立场声明[39]，也发布了实践文件[40]。欧洲高血压学会工作组强烈推荐，只要怀疑受试者有高血压，就应该进行ABPM，有必要确定持续性高血压的诊断。在日本，其2012年修订的指南对ABPM的使用提出建议，该方法不应该用于常规检查，但是，ABPM是详细评估日常血压值的一种非常好的工具。该委员会建议，ABPM应该只用于血压有较大变异性的受试者，或者疑似白大衣高血压、隐蔽性高血压或难治性高血压的受试者[41]。事实上，不使用ABPM或其他诊室外测量技术，如何能知道受试者为疑似白大衣高血压，与美国一样，由于认识到ABPM在预测脑部并发症和心血管并发症发生方面优于偶尔的血压测量，ABPM已经被纳入日本国民健康保险方案中[41]。

加拿大高血压教育计划（Canadian Hypertension Education Program）高血压管理建议发表于2010年，现在仍然有效，在≥2次诊室随访血压高于标准高血压阈值（140/90 mmHg）后，还需以下任一结果进行确诊（i）3次诊室随访的平均血压值高于阈值，（ii）ABPM，或者（iii）家庭血压测量。因此，尽管在加拿大的推荐中诊断高血压所用的血压测量技术有一定的弹性，但是，其对ABPM和家庭血压测量表示明确支持。与诊室血压测量相比（D级），推荐ABPM和家庭血压的证据水平更高（C级）。该指南认识到门诊血压的可复制性差是其内在固有特性，1级高血压确诊需要5次门诊检查，而ABPM仅需要1次。

指南在本质上倾向于保守。但是，指南工作组的大多数成员已经清楚地认识到，与诊室血压测量不准确相关的事实，以及ABPM不仅在特殊病例，而且在普通人群中的价值，不仅能更准确地评估患者的血压，而且能确诊高血压。尽管对美国全国临床优化研究所的推荐有争议[42]，但其对这一问题提供了更全面的分析，鉴于提出证据的范围，很难批驳其建议。

有基于ABPM的高血压定义和阈值吗？

准备采用ABPM替代诊室血压以诊断高血压的一个前提条件，是需要定义高血压及指导低危和高危患者治疗的全面阈值。而这些在诊室血压中已经得到公认，而且在
ABPM for Hypertension Diagnosis: Pro Case

各国的指南中基本相似（参考表6，James等）[3]。为了确定ABPM的等效值[4], 一项研究采用回归技术在超过500例患者中比较了配对的诊室血压与ABPM读数，现在ABPM也有了这些阈值[36]（表1）。澳大利亚全国心脏联盟指南推荐的这些阈值水平已得到部分验证，该方法可在准确预测140/90高血压阈值的ABPM白天血压、夜间血压和24小时血压水平等效性（表2），目前已成为国际公认[37,39,44,46,47]。另外，他们将动态血压与心脏联盟研究国际数据库中确定的数据进行紧密匹配，该研究采用与高血压ABPM阈值相当的一个预测阈值数据[31]。因此，现在已经有了在低危及高危患者中采用ABPM诊断和治疗高血压的明确而又有效的框架。

使用ABPM的障碍确实存在吗？

由于使用的方便程度、费用、患者参与，更重要的是主治医师的态度不同，ABPM对临床实践的影响在国家与国家之间并不相同。然而，对于采用ABPM替换诊室血压测量的概念，还存在抵触。针对2011年发表的英国全国心脏基金会指南中的一篇综述指出，在美国，ABPM还没有到最佳时机[31]。他们的理由是，在美国没有来自第三方付款人的合理补偿，要实现对ABPM的相似推荐，设备、工作人员和培训费用将会是压倒性的因素。澳大利亚皇家全科医师学会（The Royal Australian College of General Practitioners）的发言人也报告了相似的信息，他们支持ABPM，但是，因为费用和实践问题，如培训工作人员，而家庭血压监测更简便，故他们没有推动医疗退税政策[39]。因而，这些障碍是否真实存在的问题具有决定性意义。

| 表1. 根据诊室血压对成人高血压的分类和治疗目标[44,45], 数字来自诊室血压和ABPM之间的关系[38] |

<table>
<thead>
<tr>
<th>高血压阈值</th>
<th>诊室血压</th>
<th>24小时血压</th>
<th>夜间血压</th>
<th>白天血压</th>
</tr>
</thead>
<tbody>
<tr>
<td>1级（轻度/无并发症高血压*, JNC7中1期）</td>
<td>140/90 130/80 120/75 135/85</td>
<td>120/75 110/65 130/80</td>
<td>130/80</td>
<td>130/80</td>
</tr>
<tr>
<td>2级（中度,JNC7中2期）</td>
<td>160/100 150/90 140/85 150/95</td>
<td>150/90 140/85</td>
<td>135/85</td>
<td>135/85</td>
</tr>
<tr>
<td>3级（重度）</td>
<td>180/110 165/100 160/95 170/105</td>
<td>165/100 160/95</td>
<td>160/95</td>
<td>170/105</td>
</tr>
<tr>
<td>合并其他临床状况或终末器官损害的患者†</td>
<td>125/75 120/70 110/65 125/75</td>
<td>125/75 110/65</td>
<td>110/65</td>
<td>125/75</td>
</tr>
<tr>
<td>高血压合并蛋白尿&gt;1g/d</td>
<td>125/75 120/70 110/65 125/75</td>
<td>125/75 110/65</td>
<td>110/65</td>
<td>125/75</td>
</tr>
</tbody>
</table>

血压阈值和血压目标是基于澳大利亚全国心脏基金会的定义[36], 与JNC7相当[36], 基于经过培训的工作人员非医师测量诊室血压，预测的平均收缩压/舒张压ABPM数值取整最接近5 mm Hg，与用于高血压分段中的诊室血压水平和血压目标（上限）一致[44]。

ABP, 动态血压; ABPM, 动态血压监测; JNC7, 全国联合委员会第七次报告。

*无任何以下情况的人群：冠心病、糖尿病、慢性肾病、蛋白尿（>300 mg/d）, 卒中或短暂性脑缺血发作。
†无*所列任何情况的人群。
超过4.6万例在基层就诊的患者，以及由药店组织ABPM的近1700例患者。尽管参加药店组织ABPM的受试者患高血压的更多，但获得的数值差异在1 mm Hg之内，而且与白大衣高血压的百分比相当，具有很好的一致性[22]。然而，总值的血压特征相似。因此，由药店开展ABPM是可行的，可以为ABPM提供有用的辅助，使ABPM更加实用[23]。此外，这项研究为使用先进的中央计算机软件提供了很好的范例，如数字化收集、分析和分发ABPM记录信息，因此，在高血压的管理中减轻了医师的负担，缩短了诊室人员的工作时间，赋予患者更大的权力[22]。

### 使用ABPM诊断高血压的成本-效益比

正式的成本-效益比分析结果一致显示，使用ABPM可节省费用[34-35]。在日本，据估计，引进ABPM用于高血压的管理在10年中将节省10万亿日元，挽救近1万例患者的生命，减少近3万例中事件[57]。英国和欧洲的实施措施令人鼓舞，包括2011年在基层采用三种方法诊断高血压的成本-效益比研究，该研究显示，使用ABPM可大幅节省费用[38]。Lovibond等同事的研究[58]显示，ABPM将减少误诊，节省费用，而且，动态血压监测导致的任何费用增加均可被最佳的靶向治疗所节省的费用所抵消。在葡萄牙的基层医疗中，对疑似高血压患者广泛使用ABPM能够提高诊断的准确率，改善心血管危险分层[59]。更重要的是，与不使用ABPM的策略相比，使用ABPM能够减少医疗费用，显示出很好的成本-效益比[58]。至于美国，Krakoff估算，对于新发现的高血压受试者，将ABPM用于高血压的管理可节省3%~14%的医疗费用[58]。更重要的是，在每年总医疗费用仅有300美元时，还是节省。澳大利亚的情况与此相似，一项小规模但全面的研究显示，7年中，根据药物福利计划，总费用下降了13%，使用ABPM的费用在第1年就被不必要的治疗较少而抵消[61]。近期的一项研究提示，采用ABPM的时间治疗法，可能节省更多的费用，更好地控制白天和夜间的血压水平[22]。

#### 诊室和患者使用ABPM的费用

竞争已经使得设备的费用大幅下降，现在一些设备厂家甚至提供按次付费的合同，因此根本就没有初始投资。ABPM的费用补偿被认为是阻止ABPM日常使用的一个重要问题。在美国，从2001年开始，对于疑似白大衣高血压的患者，可以为ABPM申请医疗保险[63]。与美国相似，由于认识到ABPM在预测脑部和心血管并发症发生方面相对于偶尔血压测量的优势，以及很好的成本-效益比，ABPM也一直由日本国民健康调查方案来偿付[64]。此外，在同一项头对头比较指导抗高血压治疗的研究中，ABPM指导的治疗可减少总的处方量，与诊室血压测量相似，同时能够维持同样的血压控制，有效减轻终末器官损害[61]。在澳大利亚，对ABPM的使用没有争议，但是，在维多利亚的一些地区中心，对ABPM的广泛使用将低至40美元，对特许权持有人的广告费用低至20美元。这相当于为患者使用单一抗高血压药物治疗1个月的补助。

对于诊所，收回成本是关键问题，特别是在美国，认为ABPM的平均费用较高，但是，正确诊断高血压需要额外的会诊。当前的争议常常集中在过去我们的常规做法、通过开放新市场而做出改变的能力，竞争加剧常常不被考虑进去。通过技术改进，不仅降低费用，而且宣布将ABPM用于高血压的日常诊断就将推动其使用，同时使费用降低。因为费用太高，或者检测不那么容易获得，故我们不打算采用这一论点，而它也不会被创新者所考虑，如托马斯·爱迪森或
亨利・福特。只有先产生需求，你才能找到解决方案。一直有研究在进行成本-效益分析。

从患者的角度看，毫无疑问，选择终生抗高血压药物治疗，还是采用24小时ABPM检查来确诊，后者似乎更合适，特别是对于白大衣高血压患者。这并不意味着，这些患者一直不用治疗，因为在1~2年内他们将最终发展为真正的高血压。

有现实选择吗？

自动化诊室血压测量

最后要考虑的问题是，是否有现实的替代选择，而不必行ABPM。这种自动化的诊室血压测量技术，已有研究表明其方法可提高准确性，降低白大衣效应，可得到与白天ABP相似的血压数值。证实，已有研究提示，自动化的诊室血压测量在评估清晨血压与家庭血压测量同样有效。然而，近期一项对近的比较研究未能证实，自动化的诊室血压测量与手法测量方法相比可改善分类误差，尽管观察到白大衣效应有某种程度的减轻。

家庭或自测血压

尽管由患者在家中测量血压是一种很有吸引力的方法，但，也存在一些注意事项。对于高血压的诊断，要求患者遵循严格测量程序，早上测量两次，晚上测量两次，共持续7天，弃除第一天的数据，得到其他12次测量读数的平均值。更重要的是，根据家庭血压值不能确定夜间血压，而后者又知是预防的最强预测因素。美国评估ABPM医疗保险的专家组宣称，很重要的一点是，若不能将家庭血压作为ABPM的真正替代。如果手臂较粗患者使用的袖带大小错误（使用正常大小的袖带，而非较大的袖带），则家庭血压测量可低估了白大衣高血压，而高估了隐蔽性高血压。至于临床医生的时间和努力，家庭血压评估需要培训工作人员去培训患者，收集数据，解读结果，这些事情与ABPM需要的有不太大不同。其他问题还有读数的质量，患者的偏见，自测引起的效应问题（相当于诊室血压中的白大衣效应）。更重要的是，根据家庭血压值不能确定夜间血压，而后者又知是预后的最强预测因素。一项直接比较测量方法的研究显示，ABPM是比较家庭血压测量更优的心理血管预后因素。另一项重要的观察性研究显示，在晚上和早上家中测量血压，持续一周，共家庭血压低于白天ABP数值8/9 mm Hg。这提示，家庭血压测量不能准确反映正常的日常血压水平。因此，与ABPM结合起来，家庭血压测量有其地位，但是，除非患者不能耐受ABPM，否则不应该将家庭血压测量作为一种替代选择。这是目前多个指南的立场，包括英国指南和澳大利亚指南。

结论

在充分考虑这些问题之后，显而易见，目前有令人信服的证据支持将ABPM用于高血压的诊断。在开始抗高血压治疗或根据情况没有治疗前，如果没有仔细和准确的评估血压的非侵人性金标准，患者确实会担心。确实，最近O’Brian提出没有给患者提供ABPM的医生-法律问题，鉴于有强力证据推荐使用ABPM明确诊断高血压，或许会成为最终的转折点。这项操作并不比当前用于其他疾病的诊断方法难多少。迄今为止，其他替代选择还不够强大，ABPM的费用也不会成为妨碍其使用的原因。现在我们准备好了吗？实际上，只不过国家与国家之间的接受程度存在差异。英国已经采纳这一改变，在基层医疗中采用ABPM来确诊高血压。鉴于在患者长期健康中的重要意义，应该鼓励其他国家和地区尽早遵循他们的引导，而不是推迟。技术进步、市场竞争和按次付费合同已经取消了很多国家的困难及费用问题。然而，现实情况是，在发展中国家，现在可能还负担不起，或者还不可行。

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无。

参考文献


