Hypertension

Brief Review

What Is the Role of Ambulatory Blood Pressure Monitoring in the Management of Hypertensive Patients?

THOMAS G. PICKERING, GREGORY A. HARSHFIELD, RICHARD B. DEVEREUX, AND JOHN H. LARAGH

SUMMARY Noninvasive ambulatory blood pressure (BP) recording is now clinically available for the evaluation of hypertensive patients. It is well known that pressures measured in the office or clinic are unreliable and that repeated measurements are better at predicting outcome than are single measurements. Several studies have compared the correlation between target organ damage and different measures of BP, and in every instance ambulatory BP measurements have given better correlations than clinic readings. In one prospective study the ambulatory BP readings were more predictive of BP-related morbidity than were clinic readings. Data are now being obtained that will establish normal ranges of BP during ambulatory monitoring, against which values from patients being evaluated for hypertension can be compared. It is concluded that ambulatory BP monitoring is of clinical value for the evaluation of patients with mild hypertension. (Hypertension 7: 171-177, 1985)

KEY WORDS • blood pressure variability • target organ damage • left ventricular hypertrophy • home blood pressure

RECENT advances in medical technology have enabled the development of fully automatic, portable noninvasive blood pressure recorders that can reliably monitor changes of blood pressure over periods of 24 hours or more. The commercial availability of such recorders raises the question of their relevance to the practical management of hypertensive patients. A recent assessment by the Public Health Service concluded that the procedure is safe and effective but that "there is no evidence that ambulatory blood pressure monitoring improves the clinical management of hypertension." This assessment, however, was based on a very selective and incomplete review of the literature.

The rationale for the use of ambulatory blood pressure monitoring (ABPM) is the enormous variability of blood pressure. This variability has been amply demonstrated with both invasive and noninvasive ABPM and is not a matter of dispute. As the adverse effects of blood pressure on the circulation are thought to depend on the average level of pressure over time or possibly also on the peak levels of pressure, there is a sound theoretical reason for thinking that multiple measurements of blood pressure will be better predictors of pressure-related morbid events than single measurements. When a physician measures a patient’s blood pressure in his or her office and makes a clinical decision as a result of it, he or she is assuming that this measurement is representative of the level of blood pressure at other times. We, and others, have been able to test the validity of this assumption with the use of ABPM and have found that the correlation between clinic readings and the average 24-hour pressure level is around 0.6. This finding means that the clinic pressure can account for 36% of the variance of the 24-hour pressure. The corollary of this finding is that there is a large number of patients in whom a considerable discrepancy between the clinic pressure and the 24-hour pressure exists.

Epidemiological Evidence that Multiple Readings Are Superior to Isolated Readings

In patients with mild or borderline hypertension it is now becoming standard practice to recommend treatment only if BP remains elevated after several visits. This was done in all the recent trials of treatment of mild hypertension. The main reason for this practice is the phenomenon of regression to the mean. For
example, in the Charlottesville BP survey, 20% of adults were classified as hypertensive on initial screening, but this figure fell to 9% with repeated measurements. In the Framingham Study, three BP measurements were made at each visit, and the standard deviation for within-subject variation during one visit was approximately 7 mm Hg for systolic pressure and 5 mm Hg for diastolic. As in the Charlottesville survey, BP tended to be lower on subsequent examinations, even though these follow-up visits occurred 2 years later. More importantly, however, the average of eight measurements spaced over four visits gave a notably better prediction of future cardiovascular morbidity than did a single measurement taken on the first visit.

A similar analysis by Souchek and colleagues from the Western Electric Study showed that the mean of three readings taken at a single visit gave a substantially better prediction of future hypertension than did a single reading.

**Why Are Clinic Pressures Unreliable?**

There are two statistical criteria by which a measurement of a variable such as BP can be judged. One is the reliability—the extent to which the measurement is reproducible over time—and the other is the validity, the extent to which the measurement actually reflects the variable of interest. Many studies of clinic BP measurements have demonstrated that the usual measurement of BP is subject to a number of confounding variables. It has been known since the classic study of Ayman and Goldshine in 1940 that BP measured in the clinic by a physician is consistently higher than measurements made by the patient at home, and this has repeatedly been confirmed by ABPM studies. This pressor effect of a physician, often referred to as “white coat hypertension,” was most dramatically illustrated in a recent study by Mancia and colleagues, who found that the mere presence of a physician at a patient’s bedside induced an immediate increase in the patient’s BP of 27/15 mm Hg. The effect was less when a nurse was present. Other studies have shown that the results may also be influenced by the relationship between physician and patient, by whether the physician and patient are of the same or different sexes, and, of course, by the well-recognized effects of observer bias and digit preference. Any of these variables could change the recorded BP value by 5 mm Hg or more and, hence, determine whether or not treatment is prescribed for an individual patient. In addition to these confounding factors, the random variation of casual BP readings is very large: in one study a series of 40 readings from individuals on 20 different occasions showed a within-subject range of 25 to 30 mm Hg.

**Implications of the Therapeutic Trials in Mild Hypertension**

Although the original Veterans Administration studies provided conclusive evidence that cardiovascular morbidity and mortality in hypertensive patients (particularly from stroke) can be reduced by drug treatment, these patients were all men and most of the benefits of treatment were seen in those whose pretreatment diastolic pressures were 105 mm Hg or more. These men represented the upper extreme of the hypertensive population, while the vast majority of the estimated 20 million people with hypertension in the United States today have mild or borderline hypertension. As it is well established that cardiovascular risk is proportional to BP, such people are individually at a relatively low risk, but because of their large numbers they account for the bulk of the BP-related morbidity. The recent trials of the effects of treating such patients have in general demonstrated a reduced mortality, but a close analysis shows that the BP differences between the treated and control groups were relatively small at the end of the trial, being only 5 mm Hg in the HDFP trial. Furthermore, the elevations of BP before treatment were relatively modest; for example, a patient with a pretreatment diastolic BP of 94 mm Hg would be treated, whereas one with a pressure of 89 mm Hg would not. These considerations, which apply to the majority of hypertensive patients, imply that the way in which BP is measured is of increasing importance because the error or variability of clinic BP measurements may be much greater than 5 mm Hg.

**Analogy with Holter Electrocardiogram Monitoring**

A relevant analogy to the use of ABPM for monitoring the response to antihypertensive medication is the use of Holter electrocardiogram (ECG) monitoring for evaluating the response to antiarrhythmic therapy, particularly premature ventricular contractions. For many years this procedure has been accepted as being clinically useful and hence eligible for insurance company reimbursements, and few physicians would attempt to assess premature ventricular contractions by a conventional 12-lead ECG and rhythm strip. Like blood pressure, the frequency of premature ventricular contractions varies considerably over time. Thus, monitoring of premature ventricular contractions over short periods of time (1 hour or less) is not nearly as reliable as monitoring for longer periods in detecting complex arrhythmias and the effects of antiarrhythmic drugs can only be assessed with prolonged periods of monitoring. Even with 24-hour monitoring, the spontaneous variation is such that only if there is a change of premature ventricular contraction frequency of 75% or more can the change be attributed to the drug rather than to spontaneous variation.

**Are Noninvasive ABPM Recorders Accurate?**

It is generally agreed that intra-arterial recordings are the most accurate method for ABPM, and these have often been regarded as the gold standard. Because of their inconvenience and potential risk, however, they are unlikely ever to be of practical clinical value. The currently available noninvasive recorders are all based on the Korotkoff sound technique, in some in-
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Instruments in combination with oscillometry. These recorders therefore all have the same physiological limitations common to all sphygmanometric techniques, although they do have the advantage of avoiding such problems as observer bias and the "white coat" effect. It seems unlikely that any superior method is going to become available in the immediate future. The available recorders can be categorized in two main groups: fully automatic and semiautomatic. The former have the advantage that they require no active involvement by the patient and can be preset to take measurements at regular intervals, with the ability to take additional readings on demand. The latter require the patient to inflate the cuff manually, and as they do not require a battery-operated pump, have the advantage of being less bulky. On the other hand, they cannot obtain readings while the patient is asleep and are less likely to produce readings at regular intervals.

The two most widely used and tested fully automatic recorders are the Del Mar Avionics (Irvine, CA, USA) and the ICR (Spacelabs, Inc., Bellevue, WA, USA) recorders. The former has been demonstrated to give accurate BP readings when compared against standard mercury sphygmomanometer readings and intra-arterial pressure readings, and the latter has been validated against mercury sphygmomanometer readings. Gould and colleagues reported that the Avionics recorder was reliable for systolic pressure but overestimated the intra-arterial diastolic pressure by 11 mm Hg. They did not report correlation coefficients, however, and they found even greater deviations between manually determined auscultatory sphygmomanometric pressure and intra-arterial pressure readings. Of the semiautomatic recorders, the Remler M 2000 (Remler Corporation, Brisbane, CA, USA) has found the widest acceptance and has also been shown to have a satisfactory reliability. It should be strongly emphasized, however, that none of these recorders works in every patient and that it is essential to make calibrations against conventional sphygmomanometric measurements in every patient. Furthermore, it must be accepted that with any recorder, whether intra-arterial or noninvasive, the recordings that are obtained inevitably will include a certain proportion of readings that are artifactual, often as a result of movement, and that must therefore be edited out of the recording. Given these provisos, it can be concluded that in the majority of patients the available noninvasive recorders are sufficiently accurate to give clinically valid readings.

The reproducibility of ABPM has also been studied. Pessina and co-workers found that blood pressure readings were lower on the second of two 24-hour recordings, while others did not find appreciable changes.

Does ABPM Predict Cardiovascular Morbidity?

Given that a discrepancy exists between measurement of BP in the clinic and by ABPM, the central question is whether clinic or ambulatory readings are more predictive of the eventual consequences for the patient. In principle, this question can be answered in two ways. The first method is to compare the extent to which the two measures of pressure correlate with target organ damage, which is generally accepted to be more severe with higher levels of pressure. The second, and ultimately more important, method is to compare which measure of pressure gives a better prediction of clinical outcome.

In theory target organ damage could be measured in several ways — in the heart, peripheral vessels (including the optic fundi), and kidney. Such a comparison between ABPM and clinic BP readings was attempted in the study of Sokolow and colleagues in which target organ damage was evaluated by ECG changes of left ventricular hypertrophy, by heart size from the chest x-ray film, and by fundal changes. The overall severity of hypertensive complications was found to be more closely related to ambulatory pressure readings (r = 0.63 for systolic, 0.65 for diastolic) than to casual readings obtained in the office (r = 0.48 for systolic, 0.51 for diastolic). More recent studies have used echocardiography for evaluating left ventricular hypertrophy. This method is greatly superior to both the ECG and chest x-ray film as it is both more sensitive and more accurate. In 50 patients studied with continuous intra-arterial blood pressure monitoring in hospital, Rowlands and co-workers found higher correlations between left ventricular mass index (LVMI) and 24-hour blood pressure levels (r = 0.60 for systolic, 0.43 for diastolic) than with casual blood pressure levels (r = 0.51 for systolic, 0.30 for diastolic; Table 1). In a smaller series of 12 patients Drayer and colleagues found a correlation between ambulatory pressure and LVMI of 0.81 for systolic and 0.56 for diastolic. The corresponding correlations with casual pressure were 0.55 and 0.10 respectively. Finally, in our own series of 100 patients studied with noninvasive recorders, we also found higher correlations between ambulatory BP readings and LVMI (r = 0.50 for systolic, 0.39 for diastolic) than between casual BP readings and LVMI (r = 0.24 for systolic and 0.20 for diastolic). There is a remarkable conformity among these studies, all of which have shown that ambulatory BP monitoring is superior to casual BP recording in predicting cardiac hypertrophy. Furthermore, similar results have been obtained with invasive and noninvasive recorders.

Sokolow and colleagues also demonstrated that hypertensive retinopathy correlated more closely with ambulatory pressures than with casual pressures.

Table 1. Correlations Between Left Ventricular Hypertrophy and Casual and Ambulatory Blood Pressures

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>24-Hour SBP</th>
<th>Casual SBP</th>
<th>24-Hour DBP</th>
<th>Casual DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rowlands</td>
<td>50</td>
<td>0.60</td>
<td>0.51</td>
<td>0.43</td>
<td>0.30</td>
</tr>
<tr>
<td>Drayer</td>
<td>12</td>
<td>0.81</td>
<td>0.55</td>
<td>0.56</td>
<td>0.10</td>
</tr>
<tr>
<td>Devereaux</td>
<td>100</td>
<td>0.50</td>
<td>0.24</td>
<td>0.39</td>
<td>0.20</td>
</tr>
</tbody>
</table>

DBP = diastolic blood pressure; SBP = systolic blood pressure.
inopothy was more common in patients whose ambulatory pressures were higher than their office pressures. Littler and co-workers compared the difference between clinic and ambulatory BPs in eight untreated hypertensive patients and eight patients whose clinic readings seemed inappropriately high for their degree of target organ damage. In the former group, clinic and 24-hour BP readings were 30 mm Hg lower than clinic readings. The results of this study suggest that target organ damage is appropriate to the level of 24-hour BP but not that of the clinic BP. Similar findings were obtained by Floras and associates, who classified 59 patients with mild hypertension according to whether clinic BP was similar to or higher than ambulatory BP. Clinic BPs were the same in the two groups, but in the group in which clinic and ambulatory BPs were both elevated, target organ damage (assessed by ECG and fundal changes) was present in 64%, whereas in patients who had a high clinic BP and lower ambulatory BP target organ damage was present in only 19%.

Only one published study has related clinical outcome to ambulatory blood pressures. Perloff and co-workers followed 1076 patients for an average of 5 years. Although ambulatory and office BP readings were significantly correlated (p < 0.001), ambulatory BP readings averaged 16/9 mm Hg lower than the office BP readings. Patients were classified according to whether their ambulatory pressures were high or low relative to the office pressures. Those with ambulatory pressures higher than office pressures had a higher mortality and incidence of first cardiovascular morbidity than did those with ambulatory pressures lower than office pressures. Of particular relevance to the present discussion was the finding that the predictive power of ambulatory BP levels was greatest in those persons with milder hypertension. This is the first direct evidence that ambulatory BP monitoring can discriminate between high-risk and low-risk groups within a given level of office BP.

How Should 24-Hour Recordings Be Evaluated?

One of the reasons for the slow acceptance of the clinical relevance of ABPM is the lack of clearly defined normal values against which recordings from patients can be judged. Thus, the conventional definition of hypertension, on which we base our assessment of risk and the need for treatment, is based on clinic measurements, which as we have demonstrated are an imperfect reflection of an individual's true BP. The situation is further complicated by the fact that any distinction between hypertension and normotension is arbitrary because the relationship between cardiovascular risk and BP is a continuous one. It may be assumed that this applies equally well whether BP is measured in the clinic or by ABPM. Some studies using ABPM have failed to appreciate this, and have analyzed 24-hour recordings according to the frequency of normal and elevated readings, using an arbitrary dividing line. It is known that BP varies according to a variety of different circumstances, and as the rationale of ABPM is to measure BP during normal daily activities, it is logical to propose that such readings should be interpreted only in the context of the patients' activities at the time of the measurement. For example, a pressure of 150/90 mm Hg may be considered normal if it is recorded during mild exercise (e.g., walking), but may be thought to be high if recorded during sleep. Therefore, to make clinical sense of ABPM in patients with borderline hypertension, we need to establish the daily range of BP in normal subjects.

A limited number of studies have investigated 24-hour BP levels in normal subjects, and the results of these studies are summarized in Table 2.

### Table 2. Ambulatory Blood Pressure Ranges in Normal Subjects

<table>
<thead>
<tr>
<th>Author</th>
<th>Criterion</th>
<th>Group</th>
<th>Blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drayer</td>
<td>+ 2 SD</td>
<td>Men</td>
<td>144/90 152/94 131/85</td>
</tr>
<tr>
<td>Kennedy</td>
<td>+ 2 SD</td>
<td>Men (&lt;30 yrs)</td>
<td>133/72 129/81 131/67</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Men (&gt;30 yrs)</td>
<td>138/88 140/92 130/84</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Women</td>
<td>130/82 137/89 124/76</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Women (&lt;30 yrs)</td>
<td>134/88 141/95 123/78</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Women (&gt;30 yrs)</td>
<td>123/85 129/90 117/79</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Women (&lt;30 yrs)</td>
<td>116/83 123/85 109/75</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>Women (&gt;30 yrs)</td>
<td>122/85 129/90 117/79</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>90%ile</td>
<td>132/90 140/94 (work) 112/80</td>
</tr>
<tr>
<td>Wallace</td>
<td>+ 2 SD</td>
<td>70% Men</td>
<td>125/90 (home)</td>
</tr>
</tbody>
</table>

+ 2 SD = 2 standard deviations above the mean; 90%ile = 90% of normal subjects had values below this level of blood pressure. *Unpublished data.
conventional methods of evaluating treatment. If, however, it can be shown that there is a discrepancy between the effects of a drug on clinic and ambulatory pressures, there can be little argument that sustained reduction of BP throughout the day and night should be the accepted criterion for successful treatment. The theoretical problem with using clinic BP readings for evaluating the response to any kind of antihypertensive therapy is illustrated in Figure 1. If it is accepted that a clinic visit has a pressor effect in the majority of patients, an apparently good response to treatment, as judged by lower clinic BP reading, could occur as a result of two different mechanisms. The pressor response might be damped (Treatment A in Figure 1) without any effect on BP at other times, or there could be a uniform reduction of BP at all times (Treatment B in Figure 1). These two types of responses could only be distinguished by ABPM (or home measurements), and the clinical consequences could be quite different. We suspect that some forms of behavioral treatment (e.g., biofeedback) may produce responses of Treatment A, while pharmacological treatment produces responses of Treatment B. One such study in which these differences were observed was reported by Gould and co-workers,

It has been known for many years that home BP measurements are typically lower than clinic measurements, and it has been suggested that home BP measurement may be superior for evaluating the effects of antihypertensive therapy. The higher clinic pressure readings are probably not simply due to anxiety because they are not necessarily accompanied by a higher heart rate and may persist after repeated visits. In the past few years there has been an enormous increase in the availability of recorders with which patients can take their own BP in places other than the physician’s office. These recorders include automatic machines installed in public places such as banks and supermarkets, as well as relatively inexpensive devices available from drugstores or mail order houses with which patients can monitor their BP at home. So far, the potential impact of such devices has largely been ignored by the medical profession on the grounds that they are both inaccurate and unnecessary. The former is unfortunately too often true, and an independently conducted study of one such device (the results of which were actually included as part of the company’s promotional literature) found that the recorder had an error greater than 5 mm Hg in one-third of patients when compared with the results obtained by a conventional sphygmomanometer. Nevertheless, such machines are here to stay, and physicians must accept the fact that BP measurement can no longer be restricted to the idiosyncratic environment of the physician’s office.

It must be recognized that the results of such informal readings typically will be lower than readings taken in the conventional way, but given this difference, on which set of readings should physicians base their therapeutic decisions? The conventional wisdom is, of course, to use the clinic readings, because all the existing data used to evaluate the risks of hypertension and the benefits of its treatment were obtained with clinic readings.

On the grounds that repeated measurements of BP are more meaningful than isolated measurements, we compared BPs measured in the clinic by physicians and those taken by the patient at home with 24-hour BP measurements. As expected, we found that home BP readings were consistently lower than clinic BP measurements, but they also correlated somewhat more closely than the clinic BPs with the 24-hour BP readings. The implications of this study were, once again, that clinic BP readings are not as reliable as has been traditionally assumed and that home readings form a valuable adjunct to them.

One of the inherent limitations of home BP measures-
ments, however, is that they only reflect basal or near basal BP. It is therefore possible that an individual's BP might be normal while the subject is relaxed at home but high when the subject is under stress. This is one of the traditional arguments used in support of casual BP measurements, on the grounds that the casual BP includes a component of the response to stress as well as the basal component. Our own studies, however, do not support this view. We have found that BP measured at work is consistently higher than at home in the majority of people, which we interpret as a response to naturally occurring stress. The correlation between the increment of pressure in the clinic and at work (both relative to home BP readings) was low, however, which indicates that the pressor response to the clinic situation is not a good index of generalized hyperreactivity. Furthermore, we have two independent lines of evidence that suggest that work BP levels may have a particular pathogenetic importance. First, we have found that the correlation between 24-hour BP readings and left ventricular hypertrophy is greatest when BP is measured on a working day. Second, we found that hypertensive patients with left ventricular dysfunction (measured by radionuclide cinemangiography) showed a bigger rise in BP during work than did patients with normal ventricular function. For these reasons, it cannot be assumed that home BP measurements can obviate the need for ABPM.

Conclusion

There is little doubt that to properly evaluate something as variable as BP, repeated measurements are preferable to single measurements. Now that we are beginning to appreciate and understand this variability, it is perhaps surprising that isolated or casual measurements of BP have been such good predictors of cardiovascular risk. There is also increasing concern with the evaluation and treatment of patients with milder forms of hypertension, in whom the predictive power of casual BP readings is much poorer, even though such patients account for the majority of pressure-related morbidity. In the patient with only mildly elevated BP, the absolute increase of cardiovascular risk is small, so that more reliable estimates of BP should give a better assessment of risk and hence of the need for treatment. In every study in which ABPM has been compared with casual BP measurements, ABPM has proved superior in predicting either target organ damage or morbid events. Sufficient data from normotensive subjects is now being accumulated to use as a frame of reference against which to compare measurements from patients undergoing evaluation for borderline hypertension. In such patients ABPM may be of practical value in determining whether or not antihypertensive treatment should be initiated or adjusted.

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Hypertension. 1985;7:171-177
doi: 10.1161/01.HYP.7.2.171

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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