REVIEW ARTICLE

CURRENT CONCEPTS

Ambulatory Blood-Pressure Monitoring

Thomas G. Pickering, M.D., D.Phil., Daichi Shimbo, M.D., and Donald Haas, M.D., M.P.H.

From the Behavioral Cardiovascular Health and Hypertension Program, Department of Medicine, Columbia Presbyterian Medical Center (T.G.P., D.S.); and the Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine (D.H.) — both in New York.

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In the past 30 years, the techniques for measuring blood pressure to determine whether a patient has hypertension have undergone a substantial change. The bulk of our knowledge about the risks of hypertension and the benefits of treating it is based on the traditional method of taking a small number of readings with the auscultatory technique in a medical setting. However, such measurements, which are of enormous value on a population basis, often provide a poor estimate of risk in an individual patient for reasons such as poor technique of the observer, the "white-coat" effect (the transient but variable elevation of blood pressure in a medical setting),[1] and the inherent variability of blood pressure.[2]

Any clinical measurement of blood pressure may be regarded as a surrogate measure for the "true" blood pressure of the patient, which may be defined as the mean level over prolonged periods. Two techniques have been developed to improve the estimate of true blood pressure — ambulatory monitoring and home monitoring (or self-monitoring). We discuss only ambulatory monitoring in this review.

Techniques of Ambulatory Monitoring

Ambulatory blood-pressure monitoring was first described more than 40 years ago.[3] The currently available ambulatory monitors are fully automatic and can record blood pressure for 24 hours or longer while patients go about their normal daily activities. Most monitors use the oscillometric technique. The monitors (Fig. 1) measure about 4 by 3 by 1 in. (10 by 8 by 3 cm) and weigh about 4 lb (2 kg). They can be worn on a belt or in a pouch and are connected to a sphygmomanometer cuff on the upper arm by a plastic tube. Subjects are asked to keep their arm still while the cuff is inflating and to avoid excessive physical exertion during monitoring.

The monitors are typically programmed to take readings every 15 to 30 minutes throughout the day and night. At the end of the recording period, the readings are downloaded into a computer. Standard protocols are used to evaluate the accuracy of the monitors, and approved devices are usually accurate to within 5 mm Hg of readings taken with a mercury sphygmomanometer.[4] An up-to-date list of validated monitors is available (www.dableducational.org). Some devices have been developed that can also record 24-hour electrocardiograms, but they have not been widely used.

Ambulatory blood-pressure monitoring can provide the following three types of information, which are of potential value in the clinical field (Table 1): an estimate of the true, or mean, blood-pressure level, the diurnal rhythm of blood pressure, and blood-pressure variability. Currently, clinical guidelines exist only for estimating true, or mean, blood-pressure levels.[5-7]

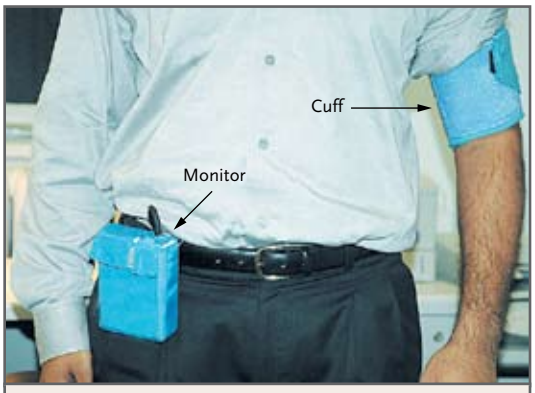

Figure 1. Ambulatory Blood-Pressure Monitor.
The sphygmomanometer cuff is connected to the monitor by means of a tube that goes under the shirt.

BLOOD-PRESSURE LEVEL

The correlation coefficient between ambulatory measurements and clinic-based measurements of blood pressure is usually about 0.5 to 0.7, but the relationship is such that at low clinic blood-pressure levels, the ambulatory blood pressure is higher, and at high clinic blood-pressure levels, the ambulatory blood pressure is lower.[8] The daytime level of ambulatory blood pressure that is usually considered the upper limit of normal is 135/85 mm Hg.[6] This cutoff is reasonable because it corresponds approximately to a clinic blood pressure of 140/90 mm Hg and, furthermore, it is the threshold above which cardiovascular risk appears to increase markedly.[9]

DIURNAL RHYTHM OF BLOOD PRESSURE

Evaluation of the time course of blood pressure over a 24-hour period can be achieved only with the use of ambulatory blood-pressure monitoring. Subjects with normotension have a pronounced diurnal rhythm of blood pressure.[10] Blood pressure falls to its lowest level during the first few hours of sleep, and there is a marked surge in the morning hours coinciding with the transition from sleep to wakefulness. The average difference between waking and sleeping systolic and diastolic pressure is 10 to 20 percent. Patients with hypertension usually have the same pattern, but the diurnal profile of blood pressure is set at a higher level.[10] In some subjects, whether they have normotension or hypertension, the normal nocturnal fall of blood pressure is diminished (<10 percent), and this is referred to as a nondipping pattern, in contrast to the normal dipping pattern. In extreme cases (e.g., patients with autonomic insufficiency), the blood pressure rises during the night. The nondipping pattern is common in blacks[11] and has multiple causes, such as a high level of activity during the day, poor quality of sleep, highly active sympathetic nervous system, use of glucocorticoids, and the presence of renal disease. Nondipping has been proposed as one reason why blacks are at higher risk for cardiovascular disease than are members of other races or ethnic groups.

BLOOD-PRESSURE VARIABILITY

There are many different ways of measuring variability, ranging from beat-to-beat changes to changes over periods of weeks or months.[12] Because the readings are taken intermittently, ambulatory blood-pressure monitoring can yield only a crude estimate of the true variations of blood pressure, other than the changes related to sleep as compared with wakefulness. The clinical significance of blood-pressure variability remains uncertain.

Table 1. Blood-Pressure Patterns That Can Be Determined by Means of Ambulatory Blood-Pressure Monitoring and Other Methods.

Variable	Ambulatory Blood-Pressure Monitoring	Clinic Blood-Pressure Monitoring	Home Blood-Pressure Monitoring
True, or mean, blood pressure	Yes	Questionable	Yes
Diurnal blood-pressure rhythm	Yes	No	No
Dipping status	Yes	No	No
Morning surge	Yes	No	Questionable
Blood-pressure variability	Yes	No	Questionable
Duration of drug effects	Yes	No	Yes

PREDICTION OF CLINICAL OUTCOMES

One trial comparing ambulatory blood pressure with conventional clinic blood pressure included patients whose hypertension had been treated at the time of the initial measurements.[13] Most such studies, however, have included patients whose hypertension was untreated at the time of the initial measurements but was treated according to the clinic blood pressure during the follow-up period. The follow-up period ranged from two to eight years, and the general finding has been that ambulatory blood pressure predicts cardiovascular events better than clinic blood pressure does.[14-22] Most of the studies used some measure of the mean level of ambulatory blood pressure as the predictor variable, but it is uncertain which component of the 24-hour blood-pressure profile gives the best prediction of risk.

The major candidates for predictors are shown in Figure 2. The most widely used has been the mean 24-hour blood pressure. Many studies have compared the predictive value of the daytime blood pressure with that of the nighttime pressure; some have shown no difference,[17,21] although others have reported that the best prediction of risk comes from the nighttime blood pressure.[20,22]

A related method of analysis is to examine dipping patterns. There is some evidence that persons with a nondipping pattern are at higher risk than those with a dipping pattern[16]; in addition, patients with an excessive morning surge of blood pressure may also be at increased risk.[23] One study that used continuous intraarterial blood-pressure monitoring[24] showed that blood-pressure variability was an independent predictor of increased left ventricular mass seven years later, even after controlling for blood-pressure level. Another prospective study, which used noninvasive monitoring, showed that increased blood-pressure variability during the day did not predict cardiovascular events after controlling for factors known to be associated with variability (e.g., age, blood-pressure level, and diabetes).[25]

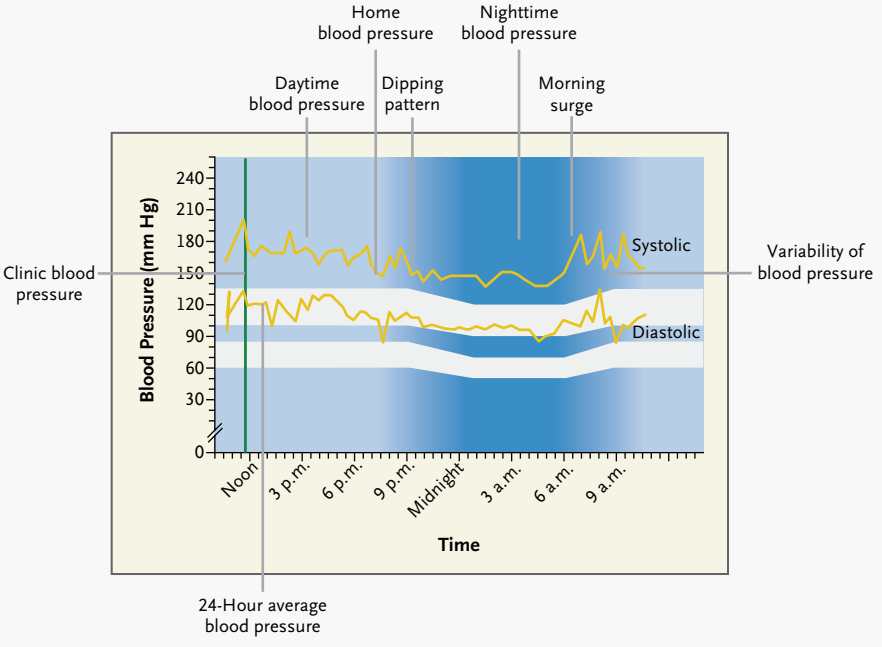

Figure 2. 24-Hour Blood-Pressure Tracing in a Patient with Hypertension.

The white zones indicate the normal ranges of systolic pressure (top) and diastolic pressure (bottom). Adapted from the dabl 24-hour Ambulatory Blood Pressure Measurement reporting system, dabl Disease Management Systems (Ireland) (www.dabl.ie).

AMBULATORY MONITORING IN OTHER CLINICAL CONDITIONS

In addition to the prediction of cardiovascular risk, ambulatory blood-pressure monitoring, when used in conjunction with clinic blood-pressure assessments, is of potential value in a variety of other clinical conditions.[26,27] Some of these conditions are listed in Table 2.

WHITE-COAT HYPERTENSION

White-coat hypertension is the only indication for ambulatory blood-pressure monitoring that has been approved for reimbursement by the Centers for Medicaid and Medicare Services in the United States. Suspected white-coat hypertension is defined as a clinic blood pressure of 140/90 mm Hg or higher on at least three occasions, with at least two sets of measurements of less than 140/90 mm Hg in nonclinic settings, plus the absence of target-organ damage. The diagnosis is important because it is generally accepted that patients with white-coat hypertension are at relatively low risk and are unlikely to benefit from antihypertensive-drug treatment. Several studies have shown that drug treatment of white-coat hypertension reduces the clinic blood pressure but has a negligible effect on the ambulatory blood pressure, which by definition is normal.[28] In addition, the only study to investigate the effects of treating white-coat hypertension on morbid events found no significant benefit.[29] Sustained hypertension may develop in some patients with white-coat hypertension, and the risk of stroke may increase after six years.[30] Therefore, long-term follow-up with repeated ambulatory blood-pressure monitoring or home monitoring is essential.

LABILE HYPERTENSION

Labile hypertension is something of a misnomer, because all hypertension is labile. However, ambulatory blood-pressure monitoring may prove helpful in some patients with a history of paroxysmal hypertension. Pheochromocytoma may be suspected in some of these patients, but the hypertension associated with this condition is not always labile.[31] A much more common cause of labile hypertension is panic attacks, which have been shown to be accompanied by surges in both blood pressure and heart rate.[32] Currently, no norms exist for determining whether blood-pressure variability over a 24-hour period is greater than normal among patients with labile hypertension.

RESISTANT HYPERTENSION

An exaggerated white-coat effect may be suspected in some patients whose clinic blood pressure remains high even though they are taking three or more antihypertensive drugs. Two prospective studies have shown that a subgroup of patients with resistant hypertension according to clinic blood-pressure criteria have normal ambulatory blood pressure and a benign prognosis.[33,34] However, these patients with apparently resistant hypertension could probably be identified with the use of home monitoring.

MASKED HYPERTENSION

In the past few years, interest has increased in the phenomenon of masked hypertension, defined as a normal clinic blood pressure and a high ambulatory blood pressure. This condition is the reverse of white-coat hypertension. The clinic blood pressure of patients with masked hypertension may underestimate the risk of cardiovascular events. A study of patients with treated hypertension showed that about one third of those seen in a hypertension clinic had masked hypertension, and over a five-year follow-up period, their relative risk of cardiovascular events was 2.28 as compared with the patients whose blood pressure was adequately controlled according to the criteria for both clinic blood pressure and ambulatory blood pressure.[34] Other studies have shown that masked hypertension in patients with untreated hypertension and often in those with

Table 2. Recommendations for the Use of Ambulatory Blood-Pressure Monitoring in Clinical Practice.*

Indication	JNC 7	WHO-ISH
White-coat hypertension	Yes	Yes
Labile hypertension	Yes	Yes
Resistant hypertension	Yes	Yes
Hypotensive episodes	Yes	Yes
Postural hypotension	Yes	No

* JNC 7 denotes the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[26] and WHO-ISH the World Health Organization–International Society of Hypertension.[27]

undiagnosed hypertension is associated with an increased rate of target-organ damage[35] and an adverse prognosis.[17] The prevalence of masked hypertension in the general population could be as high as 10 percent.[36] As with white-coat hypertension, masked hypertension may be suspected on the basis of high blood-pressure measurements taken at home, and one study has shown that masked hypertension diagnosed solely on the basis of home recordings is associated with increased mortality.[37]

POSTURAL HYPOTENSION

Postural hypotension is not an uncommon finding in older patients who become dizzy when standing for long periods and who may also have syncopal episodes. The blood pressure of patients with postural hypotension is unusually labile and depends on their body position. When such patients are supine, the blood pressure may be quite high, particularly during the night.[38] Treatment with vasopressor drugs and antigravity stockings is a compromise between permitting the blood pressure to go too low and making it go too high. Therefore, ambulatory blood-pressure monitoring is essential for evaluating optimal blood-pressure control in these patients.

EVALUATING THE RESPONSE TO ANTIHYPERTENSIVE TREATMENT

ROUTINE CLINICAL PRACTICE

Ambulatory blood-pressure monitoring is not commonly used in routine clinical practice for evaluating the response to antihypertensive treatment, mainly because of the high cost and the inconvenience of performing multiple ambulatory blood-pressure recordings. However, changes in ambulatory blood pressure correlate more closely than do changes in clinic blood pressure with the regression of left ventricular hypertrophy during antihypertensive treatment.[39]

CLINICAL TRIALS

Ambulatory blood-pressure monitoring is used frequently in clinical trials of antihypertensive drugs and, to a lesser extent, in nondrug treatment for hypertension. The reduction in blood pressure is almost always smaller with ambulatory blood pressure than with clinic blood pressure.[40] The potential advantages of ambulatory blood-pressure monitoring for assessing treatment effects in clinical trials include the ability to evaluate the duration of action of a drug and to analyze its effects on nighttime blood pressure, the need to enroll fewer patients, and better correlation of the results with clinical outcomes.[41] In contrast to their effects on clinic blood pressure, placebos have a negligible effect on ambulatory blood pressure.[42]

One goal of some trials that have compared the effects of various drugs on cardiovascular events has been to determine whether the effects are independent of the effects of the drugs on blood pressure. Ambulatory blood-pressure monitoring has often not been included in these studies, but in one instance when it was — the Heart Outcomes Prevention Evaluation Study[43] — the changes in blood pressure recorded by ambulatory monitoring in a small substudy were very different from the changes reported by clinic measurements, suggesting that the benefit derived from ramipril may have been due to its blood-pressure–lowering effects.[44]

PRACTICAL ISSUES AND REIMBURSEMENT

Ambulatory blood-pressure monitoring is not widely used in clinical practice, mainly because the expenses are often not reimbursed by insurance companies. Medicare pays between $56 and $122 per 24-hour recording session, depending on the geographic region, but only for suspected white-coat hypertension (defined as a high clinic blood pressure, the absence of target-organ damage, and evidence of normal blood pressure outside the clinic). White-coat hypertension does not warrant antihypertensive-drug treatment, but patients who receive this diagnosis undergo annual ambulatory blood-pressure monitoring. Therefore, it has been estimated that if all patients with newly diagnosed hypertension were to undergo ambulatory blood-pressure monitoring, fewer drug treatments at an annual cost of at least $300 would be necessary, resulting in a net reduction in the cost of managing hypertension.[45]

Most patients find the technique of ambulatory blood-pressure monitoring acceptable.[46] It is typically performed on a workday, when the blood pressure is often higher than on days when the patient stays at home.[47]

CONCLUSIONS AND FUTURE DIRECTIONS

Ambulatory blood-pressure monitoring is currently used only in the minority of patients with hypertension, but its use is gradually increasing. The monitors are reliable, reasonably convenient to wear, and generally accurate. Ambulatory monitoring can be regarded as the gold standard for the prediction of risk related to blood pressure, since prognostic studies have shown that it predicts clinical outcome better than conventional blood-pressure measurements. Therefore, a good case can be made for using this technique in all patients in whom hypertension has been newly diagnosed by means of clinic blood-pressure measurements. The role of ambulatory blood-pressure monitoring for diagnosing masked hypertension is uncertain.

Although ambulatory monitoring is relatively expensive in comparison with other methods of measuring blood pressure, the diagnosis of white-coat hypertension by means of ambulatory blood-pressure monitoring may reduce health care costs. Ambulatory blood-pressure monitoring is also invaluable for assessing antihypertensive treatments and should be included in studies designed to compare the effects of various drugs.

Nighttime blood pressure can be assessed only with ambulatory blood-pressure monitoring, and evidence suggests that a failure of blood pressure to decrease at night may be associated with an adverse prognosis. Also unresolved is the extent to which ambulatory blood-pressure monitoring can be supplanted by home monitoring, which was not included in most of the studies documenting the superiority of ambulatory monitoring over traditional clinic blood-pressure measurements.

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