Ambulatory Blood Pressure Monitoring: Technique and Application in the Study of Cardiac Dysfunction and Congestive Heart Failure

Ambulatory blood pressure monitoring has become a widely used method of blood pressure and heart rate evaluation in the free-living subject. Recently, ambulatory monitoring has become covered by Medicare for the evaluation of "white-coat" hypertension. Although the technique provides only intermittent readings throughout the 24-hour period, average blood pressures obtained in this way correlate well with a variety of hypertensive disease processes and are also a better prognostic marker for future cardiovascular events than office blood pressure. Ambulatory blood pressure averages also correlate well with indices of diastolic dysfunction. In patients with congestive cardiac failure and systolic dysfunction, ambulatory monitoring suggests an impaired circadian blood pressure profile with high nocturnal blood pressure. Further research is needed on the relationship between ambulatory blood pressure and cardiac dysfunction, as well as the impact of observed circadian blood pressure changes on outcome. (CHF. 2001;7:319–324) ©2001 CHF, Inc.

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Noninvasive, intermittent blood pressure monitoring, otherwise known as ambulatory blood pressure monitoring (ABPM), was first developed more than 30 years ago. There have been major technologic advancements since this early, somewhat cumbersome model, which required patient activation of each measurement. More than 25 automated, noninvasive devices are commercially available for use in children and adults,[1,2] and such devices are now more compact, fully automated, and electronically sophisticated. Furthermore, the methodology has evolved from its initial role as a research tool[2] to become an integral part of drug development, and it is increasingly used in clinical practice for the diagnosis and management of hypertension.[3]

In this review, we briefly discuss current device methodology and the use of ABPM in clinical hypertension, provide an overview of the relationship between ABPM and left ventricular hypertrophy (LVH), and review the limited contribution of ABPM in the assessment of congestive heart failure (CHF).

Device Description and Methodology

Application of ABPM to research or clinical use requires trained personnel and appropriate equipment. Monitor hook-up is ideally performed by a trained and certified technician or nurse, while data analysis and reporting are typically performed by a physician. An underappreciated fact is the critical importance of correct device placement and correlation with clinical office readings. Variables that may affect measurements include cuff placement, cuff size, and appropriate instruction of the patient wearing the monitor. Unfortunately, these simple yet critical aspects of ABPM are frequently ignored, leading to the collection of unreliable data. Patient responsibilities during the monitoring period are also important to the success of any given study (Table I).

Available ABPM devices use different methods of measuring blood pressure and a few are also capable

Table I. Patient Responsibilities During an Ambulatory Monitoring Session

- Keep arm motionless during the actual measurement
- Keep the arm roughly at heart level during the daytime measurements
- Follow a typical daily activity schedule except for heavy exercise
- Keep a detailed diary of medication intake and meal times
- Log any symptoms during the monitoring period
- Log time of getting into bed and lights out
- Log time of getting out of bed in the morning
- Report number of times patient awoke and quality of sleep
- Be able to remove the monitor if patient experiences pain or if equipment malfunctions

of simultaneous ambulatory electrocardiographic monitoring for selected patients. In an effort to reduce errors due to motion, some devices incorporate electrocardiographic R wave gating to aid in the detection of Korotkoff sounds.[4] All marketed devices in the United States must be validated to ensure that device algorithms perform comparably to standard clinical mercury column manometry.

Ambulatory blood pressure devices have been developed for two main methods of blood pressure detection: auscultatory and oscillometric. The auscultatory method uses a microphone to detect the Korotkoff sounds, while the oscillometric method detects initial (systolic blood pressure) and maximal (mean arterial pressure) oscillations of the brachial artery and calculates the diastolic blood pressure according to a validated algorithm. Both methods are less reliable in the presence of an irregular pulse and when the arm is moving during a reading. Oscillometric methods tend to work better than auscultatory devices in noisy environments. Generally, the daytime frequency of readings is every 15–20 minutes; at night, since blood pressure variability is reduced, the frequency of readings is reduced to every 20–30 minutes, which also enhances patient comfort.

Equipment Validation

Comparative studies of ABPM equipment with mercury column sphygmomanometers represent the gold standard for device validation. In an effort minimize reliance on manufacturers' reports, two acceptable standards have evolved for evaluating ambulatory blood pressure devices. The Association for the Advancement of Medical Instrumentation[5] stipulates that the test device should not differ from the mercury measurement by more than 5 mm Hg, with a standard deviation of less than 8 mm Hg. The British Hypertension Society has a more detailed protocol for evaluating automated devices[6] and grades each device according to the percentage of measurements differing from the standard by 5, 10, or 15 mm Hg or less. Monitors should also undergo routine calibration and electronic standardization at yearly intervals. A uniform, accurate, and globally accepted method of validating ambulatory monitors is needed.

Analysis of ABPM Data

The large amount of raw data from ambulatory blood pressure devices is usually downloaded to a personal computer. These data are then edited to exclude values that are thought to be artifactual. Such editing should be restricted to physiologically impossible readings to avoid removing true readings. Quality control is necessary to provide reliable data analyses. This entails not only obtaining correlative readings with the office mercury sphygmomanometer at the time of hook-up but also using a limit of at least 80% of acceptable readings after the data are collected. Ambulatory blood pressure studies collected with less than 80% acceptable readings can be misleading, especially if 2 or more hours of consecutive data are missing. Once data editing is completed, the patient's sleep time or time in bed must be considered. This allows the separation of daytime and nighttime on the data set.

Many different methods have been proposed to analyze the large amount of data provided by 24-hour measurement.[7] Summary measures are the most popular and easy to determine and include the mean and standard deviation of the 24-hour systolic, diastolic, and mean arterial blood pressures, heart rate, and double product. Such summary measures are acceptable, since they relate significantly to the hypertensive disease process, including LVH and indices of renal insufficiency.[7,8]

Furthermore, the blood pressure load may be calculated. This is the percentage of elevated readings during awake and sleep periods or over the 24-hour period. The threshold values typically used for this calculation are systolic readings above 140 mm Hg and diastolic readings above 90 mm Hg for awake periods and 120 mm Hg and 80 mm Hg for sleep readings, respectively.[8] Interval statistics, such as 12-hour interval or hourly blood pressures, early morning rise in blood pressure, and awake-sleep differences, are often calculated and displayed graphically. The load concept is interesting but suffers from saturation in

patients with significantly elevated blood pressure, such that all patients have 100% blood pressure loads. Additional useful calculations include the daytime-nighttime difference expressed as an absolute number or as a percentage of daytime averages, or the night:day ratio expressed as a percentage. Both provide a quantitative measure of the degree of dipping or nondipping of the blood pressure.

More complex approaches to smoothing the data acquired by ABPM have been advocated, including cosinor analysis, Fourier analysis with 4–6 harmonics, the spline technique, the cumulative sums method, and spectral analysis. These methods have been largely restricted to research purposes. There is no consensus as to the best approach, and average blood pressure measures appear to correlate quite well with target organ damage[9] and therefore remain the most commonly used parameters.

A source of great concern is establishment of cut-off values for diagnosing ambulatory hypertension. Ideally, such decisions should be based on outcome data or, at a minimum, on surrogate markers of hypertension damage. In the past, large patient groups or convenient samples of normotensive and hypertensive patients were studied, and arbitrary cut-offs of the 90th or 95th percentile were chosen as the limit of normal blood pressure. A summary of these data[3] led to the suggestion of thresholds for defining ambulatory blood pressure (Table II).

Ambulatory Blood Pressure and Morbidity and Mortality

One of the most consistent and important findings with regard to ambulatory blood pressure research over the past two decades has been its robust relationship to hypertensive end-organ disease.[10] This means that measuring average blood pressures using ABPM methodology has proved superior to office readings in correlating with specific hypertensive organ damage.

Table II. The Proposed Limits of Normal and Elevated Ambulatory Blood Pressure

PARAMETER	NORMOTENSION	HYPERTENSION
24-hour BP (mm Hg)	≤130/80	>135/85
Daytime BP (mm Hg)	≤135/85	>140/90
Nighttime BP (mm Hg)	≤120/70	>125/75

BP=blood pressure
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Many cross-sectional studies have linked ambulatory blood pressure to target organ damage, assessing the parameters of LVH,[11,12] microalbuminuria,[13] retinal hypertensive changes, and cerebrovascular disease.[14] The majority of these cross-sectional studies published to date have shown ambulatory blood pressure to be a better predictor of target organ damage than office measurements. This is probably a result of two factors. First, ambulatory blood pressure yields a larger number of readings than office blood pressure; second, it more truly represents the average daily blood pressure in ambulatory patients with hypertension.

A growing body of prognostic data regarding ABPM also exists. Since the early 1980s, when Perloff and colleagues[15] published their seminal report on daytime ambulatory blood pressure as a predictor of cardiovascular outcomes, several additional prospective ambulatory blood pressure studies have been completed.[16–23] The objective of these studies was to assess the predictive value of ABPM as a determinant of either cardiovascular morbidity or mortality. Despite some limitations, all of these studies have shown that ambulatory blood pressure is a far better predictor of cardiovascular events than the standard office or clinic blood pressure. Several studies, including the recently reported Syst-Eur (Systolic Hypertension in Europe) substudy on ambulatory blood pressure,[17] have also found that nocturnal blood pressure is a predictor of future cardiovascular complications. These outcome studies place ABPM on a solid foundation for routine clinical use.

White-Coat Hypertension

The finding of an entirely normal 24-hour ABPM study with elevated office readings in an untreated patient has been termed "white-coat" hypertension, implying an effect of the traditional physician attire in eliciting increases in blood pressure in the office. This pressor effect is actually somewhat generic to the medical care environment, and its detection is the most commonly cited indication for ABPM in consensus documents.[24] Depending on the definitions used, the prevalence of this condition may be as high as 10%–20%.[25]

The clinical significance of white-coat hypertension continues to be debated, with cross-sectional studies providing conflicting results.[26] In summary, the careful follow-up of white-coat hypertensive patients has shown an equal rate of development of sustained hypertension as in an age-matched group.[27] However, cross-sectional studies examining the effect of white-coat hypertension on hypertensive organ damage show conflicting results. This is likely due to the fact that various definitions are used and different patient populations have been studied. In general, when conservative cut-offs are used for awake ambulatory blood

pressure (e.g., <135/85 mm Hg or 130/80 mm Hg), the prognosis of white-coat hypertension is excellent in the short-term period of a few years.[28]

Currently, it is appropriate to use conservative cut-off values for defining hypertension on ambulatory monitoring, so that patients are not labeled as white-coat hypertensive when they are truly hypertensive. It is also prudent to treat all concomitant risk factors aggressively in such patients and reinforce lifestyle changes.

All such patients should be carefully followed, rather than assigned a definite diagnosis of normotension without follow-up.

ABPM and LVH

LVH is an important risk factor for future cardiovascular complications and it is significantly promoted by hypertension. Cross-sectional studies in hypertensive patients have, in general, shown only modest correlations between clinic blood pressure and left ventricular mass. However, ABPM correlates much better with left ventricular mass in similar studies. For both methods of blood pressure measurement, systolic blood pressure is more strongly related to left ventricular mass than is diastolic pressure.

According to a review by Appel and Stason[29] of the studies of LVH and blood pressure published before 1993, ambulatory blood pressure during work or sleep was related more to target organ damage than was clinic blood pressure. Other workers[11] have shown that nondipper hypertensive patients have excess LVH. In a large clinical trial,[12] it was also shown that regression of LVH was linked to reductions in 24-hour ambulatory blood pressure ($r=0.42$ for systolic and 0.38 for diastolic; $p<0.01$) but not office blood pressure. Thus, it is appropriate to perform ABPM in patients who have elevated left ventricular mass but normal office blood pressure. Some of these patients will demonstrate higher ambulatory than office blood pressure.

ABPM and CHF

Systolic Dysfunction. There have been no large studies examining the diurnal rhythm of blood pressure and heart rate in patients with CHF. There is also little information on whether the circadian blood pressure profile has any clinical prognostic relevance in these patients. CHF is associated with increased sympathetic nervous activity and altered baroreceptor function, both of which may influence the diurnal blood pressure rhythm.[30] Furthermore, the fluid excess present in heart failure may contribute to a blunting of nocturnal blood pressure by raising supine blood pressure. Alterations in both the level of and the circadian changes in atrial natriuretic peptide (ANP) and other hormones may also play a role in the blood pressure profiles of these patients. For ANP, there exists an antiphasic rhythm, with the peak of blood pressure rhythm occurring at the trough of the ANP rhythm.[31] Most,[31–35] but not all,[36] studies of CHF of varying etiologies have found blunting of the nocturnal decline in blood pressure.

Portaluppi et al.[31] reported altered nocturnal blood pressure in patients with CHF. These authors compared blood pressure measured every 15 minutes to changes in several hormone levels (sampled every 4 hours) over a 24-hour period in 20 patients with CHF and 10 normal volunteers. The normal volunteers showed a circadian change in ANP levels and blood pressure characterized by peak levels of ANP at 4 a.m. and low levels at 4 p.m. with normal reduction of blood pressure at night. In contrast, the heart failure patients showed no circadian changes in ANP and they had a blunted circadian blood pressure rhythm. Furthermore, no significant relationship was found between any relevant clinical or echocardiographic parameters and the extent of nocturnal dipping in blood pressure. Similarly, Kastrup et al.[35] compared the blood pressure profiles of 25 patients with congestive cardiac failure (mean ejection fraction, 17%) and 25 control subjects. The mean nocturnal decrease in systolic blood pressure was 9 mm Hg in the cardiac group vs. 18 mm Hg in the control group ($p<0.0001$) (Figure). However, Giles and colleagues[32] found an inverse relationship between absolute systolic blood pressure amplitude and plasma norepinephrine and ANP. They studied 30 patients with heart failure secondary to ischemic heart disease, with a mean ejection fraction of 25%. ABPM was performed at baseline (off vasodilator therapy) and after treatment with either captopril or lisinopril in increasing doses. Plasma norepinephrine, ANP levels, and plasma renin activity were measured at baseline as well. A strong inverse correlation was found between systolic blood pressure amplitude (50% of the difference between the daytime acrophase and the nighttime nadir, in mm Hg) and plasma norepinephrine ($r=0.51$; $p=0.004$) and ANP ($r=0.51$; $p=0.004$). No correlation was observed between the systolic blood pressure amplitude and left ventricular ejection fraction.

Caruana et al.[34] assessed 19 patients (mean age, 63 years) with CHF due to coronary artery disease and found that the day-night difference in systolic blood pressure correlated with the degree of left ventricular dysfunction. Patients with low left ven-

tricular ejection fractions had a smaller day-night blood pressure difference. The average day-night difference in the study group was 12 mm Hg, compared to 22 mm Hg in an age-matched control group. The concept of a relationship between the severity of CHF and the reduction in the day-night blood pressure difference was further supported in a younger group of 29 patients studied as part of their evaluation for heart transplantation.[33] During hospitalization, patients were studied with ABPM and with hemodynamic measurements. A control group of 22 patients also underwent ABPM while hospitalized. These authors found that more severe CHF, on the basis of hemodynamic measurements, was correlated significantly with a reduction in the amplitude of circadian blood pressure.

Moroni et al.,[36] however, were unable to show any alteration in circadian blood pressure in heart failure patients. They studied 19 patients with stage 3–4 heart failure (mean age, 57 years) and a group of age-matched controls in an outpatient setting with ABPM. Analysis was performed with the one-sample runs test followed by Fourier harmonic analysis. The authors found a persistent circadian rhythm in most of the heart failure patients, similar to that of control subjects.

When used in both normal, healthy volunteers[37] and patients with CHF,[38] digoxin significantly lowers diastolic blood pressure during sleep (4–5 mm Hg), with little or no effect on daytime blood pressure. This was discovered on use of ABPM in a placebo-controlled design. Digoxin may accomplish this by suppressing the sympathetic system activation seen in heart failure and possibly by increasing parasympathetic tone.[38]

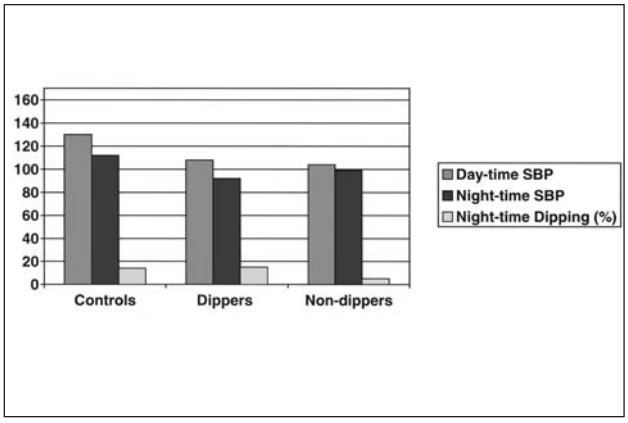

Figure. Ambulatory blood pressure results in 25 control subjects and 25 patients with congestive heart failure: dippers (n=9) and nondippers (n=16). Dippers were defined by nighttime systolic blood pressure (SBP) that decreased by more than 10%. All patients with heart failure had ejection fractions below 30%. Adapted with permission from **Scand J Clin Lab Invest.** *1993;53:577–583.*[35]

ABPM and Diastolic Dysfunction

Because abnormal diastolic function is seen early in hypertension, significant effort has been directed toward developing accurate methods to quantify such dysfunction. Various indices, primarily involving Doppler echocardiography and radionuclide ventriculography, have been developed to estimate diastolic dysfunction. Unfortunately, office blood pressure readings are poor at predicting the presence of such abnormalities; therefore, ambulatory blood pressure measurements have been the primary blood pressure parameter used to study the relationship of hemodynamic load to diastolic function.

These early disturbances of diastolic function are certainly common, and the prevalence of asymptomatic left ventricular filling abnormalities in adults with hypertension without LVH is about 20% in patients below 50 years of age.[39] In one study,[40] when the daytime blood pressure was <130/85 mm Hg, no evidence of diastolic abnormalities was found. White et al.[40] have shown that the blood pressure load is an excellent method for delineating the presence or absence of an abnormal diastolic filling rate. Galderisi et al.[41] analyzed the effects of ambulatory and office blood pressure on diastolic function in 125 subjects with a mean age of 46 years. They found that age, nighttime blood pressure, and heart rate were predictors of left ventricular filling impairment. Similarly, Verdecchia et al.[42] studied the effects of clinical parameters on left ventricular diastolic filling abnormalities in a group of 145 hypertensive subjects and 105 healthy, normotensive volunteers. Using a multivariate approach, they showed that both age and ambulatory blood pressure were significantly related to these indices. Clinic blood pressure was not a determinant of these abnormalities. Multiple clinic blood pressure readings improve the correlation between office blood pressure and the presence of diastolic dysfunction.[39]

Conclusions

Our current knowledge of ambulatory blood pressure and its relevance in cardiac systolic and diastolic dysfunction and CHF is limited. Most studies that have examined the circadian blood pressure profile have found blunting of the decline in blood pressure during sleep. In other hypertensive populations, this alteration in nocturnal blood pressure has been demonstrated to be a negative cardiovascular prognostic factor. It is tempting to speculate that this may also be true in patients with CHF, but this remains a hypothesis to be tested. A growing

interest in improved control of blood pressure should stimulate research into the clinical relevance of circadian blood pressure changes in this patient population.

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