



HHS Public Access

Author manuscript

J Hum Hypertens. Author manuscript; available in PMC 2011 October 01.

Published in final edited form as:

J Hum Hypertens. 2011 April ; 25(4): 250–255. doi:10.1038/jhh.2010.66.

Indication-specific 6-hour systolic blood pressure thresholds can approximate 24-hour determination of blood pressure control

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Abstract

Ambulatory blood pressure monitoring (ABPM) is an accurate method for evaluating hypertension, yet its use in clinical practice may be limited by availability, cost, and patient inconvenience. The objective of this study was to investigate the ability of a 6-hour ABPM window to predict blood pressure control, based on that of the full 24-hour ABPM session across several clinical indications in a cohort of 486 patients referred for ABPM. Sensitivities and specificities of the 6-hour systolic blood pressure mean to accurately classify patients as hypertensive were determined using a fixed reference point of 130 mmHg for the 24-hour mean. For four common indications in which ABPM was ordered, prediction tables were constructed varying the thresholds for the 6-hour mean to find the optimal value that best predicted the 24-hour hypertensive status as determined from the full 24-hour interval. Using a threshold of 137 mmHg for the indications of borderline hypertension, evaluation of current antihypertensive regimen and suspected white-coat hypertension, sensitivity and specificity ranged from 0.83–0.88 and 0.80–0.88, respectively, for the ability of 6-hour ABPM to correctly categorize hypertensive status. Using 133 mmHg as the threshold for treatment resistance resulted in a sensitivity and specificity of 0.93 and 0.83, respectively. We conclude that a shortened ABPM session of 6 hours can be used to accurately classify blood pressure as controlled or not, based on the results of a 24-hour session. The optimal 6-hour threshold for comparison depends upon indication for referral.

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Presented in part at the 21st annual meeting of the American Society of Hypertension, May 2008. New Orleans, LA.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Keywords

ambulatory blood pressure; hypertension; short-term

INTRODUCTION

Out-of-office blood pressure assessments, including 24-hour ambulatory blood pressure monitoring (ABPM) and home/self blood pressure measurement, are important techniques to improve estimates of the true blood pressure of patients with hypertension.^{1,2} Compared to traditional office blood pressures, these measurements more reliably predict the risk for target organ damage.^{3–6} In the case of ABPM, the improved ability to predict risk of cardiovascular events is due to a number of features; namely, that ABPM eliminates observer variability and digit preference often seen in clinical practice, and more importantly, provides assessment of blood pressure throughout the nighttime hours.⁷ Out-of-office blood pressure assessment can be helpful in the evaluation of patients with suspected white-coat or borderline hypertension, apparent drug resistance, orthostatic hypotension, and episodic hypertension.⁸

The routine use of ABPM in clinical practice presents a logistical challenge for some patients. First, ABPM requires a significant time commitment, which may interfere with routine daily activities including work and recreation. Secondly, some patients report discomfort associated with the procedure, including increased nocturnal awakenings.^{9,10} Third, ABPM may not be accurate in some patients such as those with cardiac arrhythmias, very large arms, or poor musculature of the upper arms.^{11,12} Lastly, the average cost of an ABPM session is approximately \$300–500 and is not uniformly reimbursed by insurance carriers. Collectively, these limitations are barriers to more widespread use of ABPM in primary care settings. The valuable information obtained from ABPM makes it important to refine strategies for how best to incorporate ABPM into clinical practice.

We previously demonstrated that the mean systolic blood pressure of a shortened window (6-hours) of an ABPM session can approximate the mean systolic blood pressure of the full 24-hour ABPM session.¹³ Shorter ABPM sessions could be a useful strategy when out-of-office assessments are desired, but are otherwise unavailable or unable to be performed to their complete extent. We hypothesized that the utility of the 6-hour ABPM window we described previously could be optimized based on the clinical indication for which the patient was referred for ABPM. The purpose of this study was to examine the agreement of the 6-hour interval mean systolic blood pressure with the 24-hour mean systolic blood pressure across several clinical indications of referral. We also sought to identify the optimal threshold for the shortened window to accurately classify a patient's blood pressure as controlled or uncontrolled as determined from the full ABPM session.

POPOULATION and METHODS

Study Population

Data were reviewed from a cohort of ABPM sessions previously performed by the ABPM referral service of the Family Care Center of the University of Iowa Hospitals and Clinics. This service accepts consults from the outpatient clinics of Departments of Family Medicine and Internal Medicine, and is co-directed by a board-certified family physician and a board-certified clinical pharmacotherapist. For each consult, a member of the ABPM team meets with the patient to provide standardized education about the session, and fits the patient with the appropriate sized blood pressure cuff as determined by arm circumference according to the American Heart Association guidelines for blood pressure measurement.¹⁴ Blood pressure readings were obtained every 20 minutes during the daytime (0600 to either 1800, 2000, or 2200 hours), and every 30 minutes during the nighttime (1800, 2000, or 2200 to 0600 hours). The times of initiation and termination of the ABPM sessions were not standardized for each patient to allow flexibility in scheduling and availability of the monitors.

Our study population was a convenience sample of all ABPM sessions processed by the clinic as part of routine clinical practice from its inception in January 2001 through June 2007, coinciding with our previous analysis.¹³ Three SpaceLabs 90217 monitors (SpaceLabs Medical, Inc, Redmond, WA) were used for all ABPM sessions to insure uniformity. These monitors meet both the Association for the Advancement of Medical Instrumentation and British Hypertension Society standards for accuracy.¹⁵ Blood pressure data obtained from the monitors was retrieved using the SpaceLabs ABP Report Management System software platform (v. 1.03.11 and v 2.00.06).

For this analysis, sessions were grouped according to the four most common indications of referral to our service: borderline hypertension (not currently treated but with a series of variable office blood pressures in both the normal and elevated range), evaluation of blood pressure control on mono or dual therapy, suspected white-coat hypertension, and treatment resistance (receiving treatment with three or more antihypertensives). Duplicate ABPM sessions for an individual patient were excluded, as were ABPM sessions referred to the clinic for indications other than the four specified above. Given the unknown variance for the agreement between the 6-hour and 24-hour means across different clinical indications, no formal power calculation was employed. The study was approved by the institutional review board of the University of Iowa.

Statistical Analysis

Our analysis sought to describe the agreement between a 6-hour mean systolic blood pressure and that of the 24-hour mean, and to identify the optimal threshold based on indication of referral for the ability of the 6-hour mean accurately classify whether the patient's systolic blood pressure was controlled. We examined only the agreement for systolic blood pressure since it is the measurement most closely associated with the risk for cardiovascular events in the age distribution of our population typically referred for ABPM.

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To calculate the 6-hour and 24-hour interval mean systolic blood pressure, the mean systolic blood pressure for each individual patient was calculated for these time periods and then the mean of those means was determined. The first hour (“white-coat window”) of each session was excluded from the 6-hour interval mean and the 24-hour mean since it was significantly higher regardless of the time of day the session was started. Although the 6-hour interval mean is comprised of only 5-hours of data, we refer to the shortened time interval as a “6-hour” interval mean throughout this report. This is because the white-coat window occurred regardless of the time the device was started, and a monitor would in all cases need to be worn for 6 hours to obtain the 5 hours of data necessary to make the evaluation. When encountered, missing hourly data were accommodated with likelihood-based methods.

To describe agreement of the 6-hour mean and the 24-hour mean across indication groups, area under the receiver operating curve (ROC), kappa statistics (percent agreement), and percent absolute value of relative differences were calculated. Sensitivity and specificity of the 6-hour mean to accurately classify patients as hypertensive based on their 24-hour systolic blood pressure mean were determined using a fixed value of 130 mmHg as the 24-hour mean reference point. Although there are no firmly established guidelines for normal and abnormal ABPM values, the reference point of 130 mmHg for the 24-hour mean was chosen because a systolic blood pressure of 130 mmHg or less for the 24-hour mean is generally considered within normal limits.¹⁴ A 6-hour mean systolic blood pressure above 130 mmHg would indicate uncontrolled systolic blood pressure for the remainder of the 24-hour session, while below 130 mmHg would indicate controlled systolic blood pressure. Prediction tables were generated by varying the systolic blood pressure thresholds for the mean of the 6-hour interval in order to determine the optimal systolic blood pressure threshold associated with the most favorable sensitivity and specificity for predicting the hypertensive status as determined from the 24-hour mean. All statistical analyses were performed using SAS 9.0 (SAS Institute) and R (The R Project for Statistical Computing, www.r-project.org).

RESULTS

A total of 569 ABPM sessions were reviewed for inclusion in this study. Duplicate sessions from individual patients were excluded (n=39), as were 44 ABPM sessions referred to the clinic for indications other than those identified in this study. Table 1 shows the demographics of the patient population. The mean age was 52.7 years, and 50% of patients were male. The average session duration for ABPM lasted 22.4 hours (range 19.1–25.7 hours). The mean office blood pressure taken before the ABPM session was 150/83 mmHg. A total of 486 ABPM sessions were included in the final analysis, which included 126 for borderline hypertension, 159 for evaluation of blood pressure control on current therapy, 137 for suspected white-coat hypertension, and 64 for treatment resistance.

Figure 1 illustrates the agreement between the 6-hour mean systolic blood pressure and the mean of the full 24-hour ABPM session over a range of thresholds for the different referral groups. Analysis of the kappa statistics indicated substantial agreement for mean 6-hour systolic blood pressure threshold ranges of 135–140 mmHg for the indications of borderline hypertension, evaluation of blood pressure control on current therapy and suspected white-

coat hypertension (Groups I–III). However, resistant hypertension (Group IV) saw the highest agreement and kappa around 132–133 mmHg.

Based on the kappa statistics determined in Figure 1, the sensitivity and specificity of a range of 6-hour thresholds used to classify systolic blood pressure as controlled or not based on the 24-hour mean, were calculated. These results are shown in Table 2. Using a 6-hour systolic blood pressure mean threshold of 137 mmHg for Groups I–III, and 133 mmHg for Group IV, achieved a sensitivity/specificity of 0.88/0.88 for Group I, 0.83/0.85 for Group II, and 0.86/0.80 for Group III, respectively. A threshold of 133 mmHg for Group IV resulted in a sensitivity/specificity of 0.93/0.83.

Table 3 summarizes the ROC statistics, percent agreement, percent absolute relative difference, sensitivity, specificity and corresponding likelihood ratios using systolic blood pressure thresholds of 137 mmHg for Groups I–III, and 133 mmHg for Group IV. Using these thresholds, the corresponding positive and negative likelihood ratios were 7.27 and 0.13 for Group I, 5.34 and 0.21 for Group II, and 4.23 and 0.18 for Group III, respectively. With 133mmHg as the reference for Group IV, a positive and negative likelihood ratio of 5.55 and 0.09 was calculated.

DISCUSSION

This study suggests that a 6-hour ABPM window can be used to accurately classify a patient's hypertensive status as determined from their 24-hour mean systolic blood pressure for four common indications of referral for ABPM. We found that the optimal 6-hour threshold used to categorize patients as hypertensive or controlled varied across these indications. Using the 6-hour mean systolic blood pressure threshold of 137 mmHg for the three indications of borderline hypertension, evaluate blood pressure control on current therapy, and suspected white coat hypertension, we found relatively high sensitivity and specificity for this 6-hour mean to accurately classify overall hypertensive status based on the full 24-hour results. A lower threshold of 133 mmHg was necessary for patients referred for resistant hypertension. This difference is likely due to the lack of the 6-hour interval to include nighttime blood pressures since nearly all patients were initially set up during morning hours, as well as the likelihood of patients referred for resistant hypertension having overall higher mean systolic blood pressures.

Measurement of blood pressure is an important surrogate for the determination of cardiovascular risk. Office-based sphygmomanometry remains the gold standard upon which most treatment decisions are made. However, office-based measurements are subject to numerous limitations including observer bias, terminal digit preference, and failure to detect white-coat hypertension, all of which can lead to erroneous treatment decisions.^{17,18} Out-of-office measurements, including home/self-monitoring and ABPM, can enhance determination of a patient's true blood pressure level but are not always readily available nor are all patients able to comply with the request to obtain home/self-measurements.

A proposed alternative to a full 24-hour ABPM session has been shorter duration sessions that can predict the 24-hour mean blood pressure.^{13,19–21} Truncated ABPM sessions were

first shown to be predictive of full 24-hour ABPM sessions in 1982.¹⁹ A small study of 6 hypertensive patients compared the mean blood pressure of serial readings over a 2-hour period, 3 consecutive readings, and one single reading to the mean blood pressure of the 24-hour ABPM session. The study concluded that the average blood pressure determined by the 2-hour monitoring period was more consistent with the full 24-hour monitoring session than the single reading.

Larger studies have since compared shorter ABPM sessions to a full 24-hour session. 13,20,21 Sheps, et al. found that a shortened ABPM session of 6 hours can predict the daytime mean blood pressure in a study of 126 normotensive patients and 168 mildly hypertensive patients not on treatment.²⁰ Chanudet et al. evaluated the time span that most accurately predicted 24-hour mean blood pressure in 254 patients with normal or borderline elevated office blood pressure.²¹ They concluded that 1 and 2-hour intervals were poor predictors of mean 24-hour blood pressure but 4-hour intervals taken between 1000–2200 hours accurately estimated the daytime mean blood pressure. In a retrospective analysis of over 1000 ABPM sessions, we previously demonstrated that a 6-hour ABPM mean could approximate the mean blood pressure of a full 24-hour monitoring session.¹³ Our current study expands the utility of these results by examining agreement based upon the indication for ABPM referral. To our knowledge, it is the first study to analyze the predictive value of a shortened ABPM session across different clinical indications of referral.

Several limitations should be noted in our analysis. First, we examined only the first 6 hours of the session, which does not include the nighttime period, and period of strong predictive value for cardiovascular events.⁷ Future studies can vary the constituents of the 6-hour period, such as inclusion of hours later in the day or early evening, to improve agreement of a 6-hour mean with the 24-hour mean. Secondly, our study was a retrospective analysis of previously performed ABPM sessions. Prospective studies of a 6-hour session compared to that of a full session would be necessary to validate the predictive ability of the shorter session to accurately classify hypertensive status, as well as correlate with target organ damage. Finally, the predictive ability of the 6-hour period may vary significantly depending on the population in which it is employed. An unintended consequence of advocating 6-hour ABPM sessions could be more widespread use in populations where the underlying pre-test probability of having hypertension (or being uncontrolled) exists. A lower overall prevalence of hypertension in the population in which the test is ordered would result in a lower post-test probability and limit usefulness.

The advantages of out-of-office blood pressure measurements are numerous. For ABPM, a 24-hour period of evaluation is preferred as it is the basis upon which ABPM has demonstrated greater predictability for cardiovascular events than office measurements. However, ABPM is not available in all patients, can be associated with increased expense, and will not be accurate in patients with arrhythmias or extremes of body habitus. Several studies have observed that a series of carefully performed home measurements can provide similar agreement to ABPM and correlate with target organ damage.^{5,6} While home/self measurements may be a preferred alternative, not all patients comply with the request to obtain them. When home/self-measurements are unavailable, a limited 6-hour ABPM session may be an acceptable alternative for predicting the patient's hypertensive status to

make decisions about treatment. Such a session could potentially increase patient acceptance and physicians' inclination to recommend such procedures, although this would need further prospective study. It is important to remember that a shortened ABPM session will not reflect the nighttime blood pressure, and would not be preferred when evaluation of circadian blood pressure variation is desirable.

A shortened ABPM session of 6 hours can accurately predict a patient's hypertensive status as determined from their 24-hour ABPM session. The optimal systolic blood pressure threshold for comparison depends upon the indication for referral. Further prospective research is necessary to determine if a shortened ABPM session maintains its ability to predict target organ damage and cardiovascular risk, or provides an advantage over home/self-monitoring.

Acknowledgments

Funding: This work was supported in part by the National Heart, Lung, and Blood Institute (1R01HL069801-01A1).

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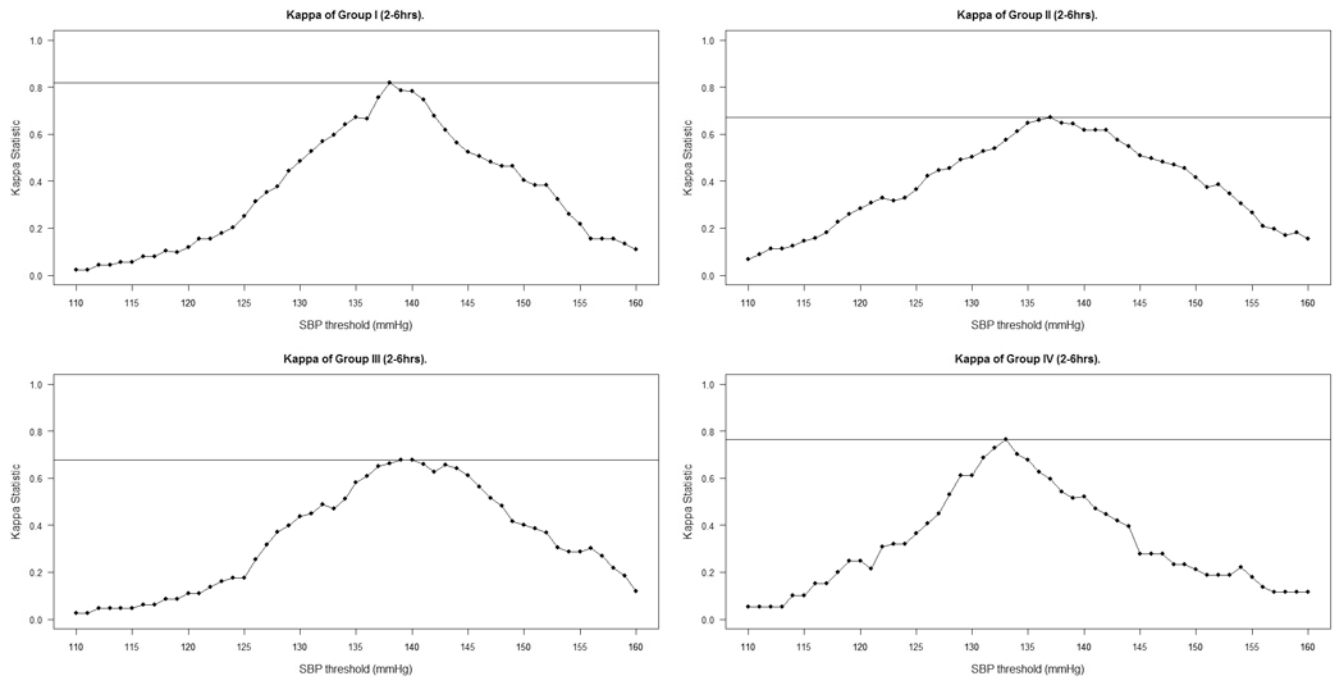


Figure 1.

Kappa statistics for agreement of the 6-hour mean systolic blood pressure with the 24-hour mean using varying 6-hour thresholds. (Fixed systolic blood pressure value of 130 mmHg used as the 24-hour reference point for controlled vs uncontrolled.)

Group I: borderline hypertension

Group II: evaluation of blood pressure control on mono or dual therapy

Group III: suspected white-coat hypertension

Group IV: treatment resistance

SBP: systolic blood pressure

Table 1

Demographic characteristics of the study population.

Characteristic	Mean ± SD
Age (years)	52.7 ± 15.9
Body Mass Index (kg/m ²)	29.5 ± 6.6
Session Duration (hours)	22.4 ± 3.3
Clinic Blood Pressure (mm Hg)	150/83 ± 20/11
	No. (%) of Patients
Male	265 (50)
Successful sessions *	449 (84.7)
Indication for test	
Suspected white coat hypertension	137 (25.8)
Borderline hypertension	126 (23.8)
Evaluation of blood pressure control on therapy	148 (27.9)
Resistant hypertension	64 (12.1)

* defined as 80% of attempted readings resulting in a successful measurement SD: standard deviation

Table 2

Sensitivity and specificity of the 6-hour ABPM mean to predict controlled or uncontrolled blood pressure as determined from the 24-hour ABPM. (Fixed systolic blood pressure value of 130 mmHg used for the 24-hour mean reference point of control vs uncontrolled.)

Indication Group	6-hour Systolic Blood Pressure Threshold (mm Hg)										
	131	132	133	134	135	136	137	138	139		
I	Sensitivity	0.94	0.94	0.94	0.94	0.90	0.88	0.88	0.85		
	Specificity	0.62	0.66	0.69	0.73	0.76	0.78	0.88	0.93		
II	Sensitivity	0.87	0.87	0.87	0.85	0.85	0.83	0.80	0.79		
	Specificity	0.67	0.68	0.71	0.76	0.80	0.81	0.85	0.86		
III	Sensitivity	0.95	0.92	0.89	0.89	0.89	0.87	0.86	0.84		
	Specificity	0.51	0.58	0.59	0.63	0.70	0.74	0.80	0.82		
IV	Sensitivity	0.95	0.93	0.93	0.88	0.83	0.75	0.73	0.68		
	Specificity	0.71	0.79	0.83	0.83	0.88	0.92	0.92	0.92		

Group I: borderline hypertension

Group II: evaluation of blood pressure control on mono or dual therapy

Group III: suspected white-coat hypertension

Group IV: treatment resistance

Table 3
Summary of the agreement of the 6-hour systolic blood pressure mean with 24-hour mean.

	Group			
	I	II	III	IV
ROC (SE), 6-hr vs 24-h (using 130 mmHg as reference standard)	0.932 (0.027)	0.895 (0.025)	0.901 (0.028)	0.909 (0.041)
6-hour SBP Threshold (mmHg)				
κ (SE)	0.657 (0.060)	0.672 (0.059)	0.650 (0.065)	0.600 (0.096)
% Agreement (SE)	88.9 (2.80)	83.6 (2.93)	82.5 (3.25)	79.7 (5.03)
Sensitivity	0.88	0.83	0.86	0.73
Specificity	0.88	0.85	0.80	0.92
LR+	7.27	5.34	4.23	8.70
LR-	0.13	0.21	0.18	0.30
κ (SE)				0.765 (5.03)
% Agreement (SE)				89.1 (3.90)
Sensitivity				0.93
Specificity				0.83
LR+				5.55
LR-				0.09
% absolute value of relative differences (SE)	0.07 (0.004)	0.06 (0.004)	0.07 (0.004)	0.06 (0.006)

κ= Kappa; SE= standard error; LR= likelihood ratio; SBP=systolic blood pressure

Group I: borderline hypertension

Group II: evaluation of blood pressure control on mono or dual therapy

Group III: suspected white-coat hypertension

Group IV: treatment resistance

Table 4

Summary Table

What is known about this topic	What this study adds
Measurements from 24-hour ambulatory blood pressure monitoring (ABPM) strongly predict risk of cardiovascular events.	6-hour ABPM can approximate the mean systolic blood pressure of a full 24-hour monitoring session.
ABPM provides useful information in the evaluation of suspected white-coat hypertension, treatment resistance, orthostatic hypotension, and episodic hypertension.	A 6-hour ABPM session can accurately predict blood pressure control as determined from a 24-hour session.
Not all appropriate candidates for ABPM are able to undergo the procedure as it is associated with significant cost, time commitment, and occasional discomfort.	The ability of 6-hour ABPM to predict 24-hour control is dependent on the indication for referral and the associated reference threshold.

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