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Abstract—White coat hypertension (WCH) is common in referred hypertensive patients. Ambulatory blood pressure monitoring (ABPM) is not free from the white coat syndrome. We examined the use of the elevation of the first and last measurements of ABPM for diagnosis of WCH in a hypertensive population that had been referred to a hospital-based hypertension unit. Data were obtained on 1350 patients for clinic and ABPM parameters. WCH, as diagnosed by conventional clinic blood pressure (BP) measurement, was compared with a variety of alternative methods determined from ABPM. In all cases, mean daytime pressure was <135 mm Hg/85 mm Hg with an elevation of clinic BP ≥140 mm Hg systolic or 90 mm Hg diastolic. The definitions tested for this elevation were first hour mean pressure, first reading, maximum reading in first hour, last hour mean pressure, last reading, maximum reading in the last hour and maximum reading in first or last hour. Elevation of the maximum pressure in the first hour or last hour above 140 mm Hg systolic or 90 mm Hg diastolic showed a high level of agreement ($\kappa=0.91$) with classical WCH for diagnosis of the white coat syndrome. Termed ambulatory white coat hypertension, patients with this finding were older than classic white coat patients and had higher daytime ($127\pm6/78\pm5$ mm Hg versus $121\pm5.5/74\pm6$ mm Hg, $P<0.005$ for systolic and diastolic) and nighttime ($114\pm11/67\pm8$ mm Hg versus $106\pm9/61\pm6$ mm Hg, $P<0.005$ for systolic and diastolic) pressures. They also had a significantly greater Sokolow-Lyon index (leads V_1+V_5, 21 ± 7 mV versus 18 ± 6 mV). Elevation of BP above 140 mm Hg systolic or 90 mm Hg diastolic in the first or last hour of monitoring diagnoses patients with a white coat response in whom there is a higher BP profile than in patients with classic white coat response alone. We suggest, therefore, that this is a better measure of the white coat phenomenon. (*Hypertension*. 1999;34:267-272.)

Key Words: blood pressure monitoring, ambulatory ■ hypertension, white coat

White coat hypertension is a common finding in hypertensive populations and in the population at large. The incidence has variably been recorded between 12% and 50%, depending on definitions.[1] The importance of the condition lies in the relatively benign cardiovascular risk with which it is associated compared with established hypertension.[2] The phenomenon of white coat hypertension may reflect an abnormally vigorous sympathetic response to the environment of the measurement,[3] especially the presence of the measuring nurse or physician.[4]

Ambulatory blood pressure (BP) is the most frequent mechanism used in measuring the presence of the white coat effect. The standard definition of white coat hypertension is an elevation of clinic pressure with a normal daytime ambulatory profile.[5] However, our experience has been that the initial few measurements on the ambulatory monitor, and, indeed, the final measurement, which reflect the patient's attention to attaching and removal of the monitoring device, respectively, are frequently abnormal also. A typical ambulatory monitor recording from such a patient is shown in Figure 1. This study has been undertaken, therefore, to establish the clinical usefulness of the first and last measurement of ambulatory monitoring in the diagnosis of white coat hypertension.

Methods

The patient population used in this study was a cohort of 1350 patients, drawn from a total database population of 2425 patients, who attended the "shared care" hypertension management program in our institution for assessment of their hypertension. The patient exclusion protocol is depicted in Figure 2. All patients were classified as hypertensive if the referral physician-recorded clinic BP was ≥140 mm Hg systolic or 90 mm Hg diastolic.[6] None of the patients were on vasoactive medications at the time of monitoring, and subjects were excluded if antihypertensive drugs had been taken within 2 weeks of the study.

Upon arrival for ambulatory monitoring, the patient had clinic BP measurement performed by the attending nurse in the BP unit. BP was measured in the nondominant arm after 5 minutes of quiet sitting; the BP measurement was taken in accordance with the recommendations of the British Hypertension Society.[7] Only patients in whom both this clinic BP and the original referral BP were above normal were included in the analysis. ECG was performed with the use of a standard 12 lead placement within 1 week of attendance at the BP unit, and left ventricular voltage criteria for ventricular mass

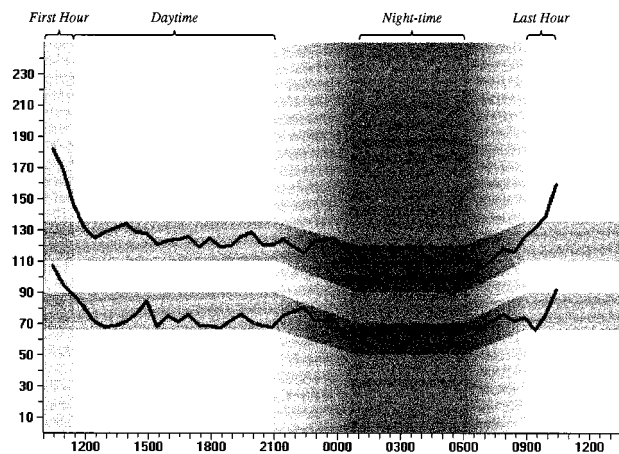*Hypertension* is available at http://www.hypertensionaha.org

Figure 1. Typical ambulatory BP pattern from a patient with white coat hypertension.

were determined with Sokolow-Lyon V_1+V_5 and V_1+V_6 voltage summation.

Ambulatory BP monitoring was performed with the SpaceLabs 90207 ambulatory blood pressure monitor (ABPM).[8] The monitor was applied to the nondominant arm between 9:00 AM and noon. The patient was instructed to perform normal activities between measurements but to rest the arm at heart level during measurements. Monitors were programmed to measure BP at 30-minute intervals

Figure 2. Flow chart for patient selection process.

TABLE 1. Acceptable BP Ranges

Parameter	Minimum (mm Hg)	Maximum (mm Hg)
SBP	70	285
DBP	40	200
MAP	60	240
PP	16	

day and night. The monitor was removed the next day after 8:00 AM, and the data were transferred to a personal computer and loaded into a specialized software package (DABL).[9] Mean systolic BPs (SBPs) and diastolic BPs (DBPs) were calculated for the initial, daytime, nighttime, and final hour periods. The initial period was defined as the first hour of recording. Daytime was defined as the hours between 9:00 AM and 9:00 PM (excluding the initial period), and nighttime as the hours between 1:00 AM and 6:00 AM. The transition time (9:01 PM to 0:59 AM) was not included in the estimation of day and night mean pressures because this period represents time during which bed rest is inconsistent and, therefore, cannot be categorized reliably.[10] Readings obtained during the second day of recording were not included in the definition of the daytime period. Acceptable BP limits are shown in Table 1.

White coat parameters examined in the present study are defined in Table 2. The first reading is the reading obtained by direct actuation of the monitor by the attending nurse when the patient was still in the BP unit. The last reading is the reading obtained just before removal of the monitor by the patient or by the attending nurse when the patient was in the BP unit the next day for removal of the unit. Recordings that did not show data for nighttime BP were not included in the analysis. Furthermore, patients on night shift work, or within 4 weeks of completing night shift duty, were not included in the analysis because shift work may result in an artificially reversed diurnal rhythm.[11] Recordings were not included if there were <14 valid readings during the day or <7 valid readings during the night. The device used was validated by and passed both the Association for the Advancement of Medical Instrumentation[12] and British Hypertension Society[13] protocols, and all instruments were serviced regularly to ensure that they maintained their performance.

Statistical Analysis

The ABPM data were processed by use of a commercially available statistical analysis software package (SPSS, SPSS Inc). Agreement between categorical variables was determined by calculation of the kappa (κ) statistic. Continuous data were compared using the Student t test.

Results

Records from 1350 patients were available for studies, all of whom, by definition, had elevated physician referral pressures and those pressures were confirmed on repeat measurement by the nurse in the BP unit. Of the initial 2425 patients noted to be hypertensive by their physician, 2244 (92.5%) were again found to be hypertensive by the nurse. Reasonable uniformity was found among the start time (minimum, 8:20 AM; 5th percentile, 9:08 AM; median, 10:41 AM; 95th percentile, 12:21 PM; maximum, 1:52 PM), end time (minimum, 8:05 AM; 5th percentile, 8:50 AM; median, 10:30 AM; 95th percentile, 12:30 PM; maximum, 4:49 PM) and duration in hours (minimum, 20 h, 59 min; 5th percentile, 22 h, 53 min; median, 23 h, 56 min; 95th percentile, 24 h, 51 min; maximum, 30 h, 09 min) for ambulatory recordings. The mean age was 50.9 ($\pm$12.4) years, and 56.6% of the patients were female. Table 3 shows the baseline clinical and pressure
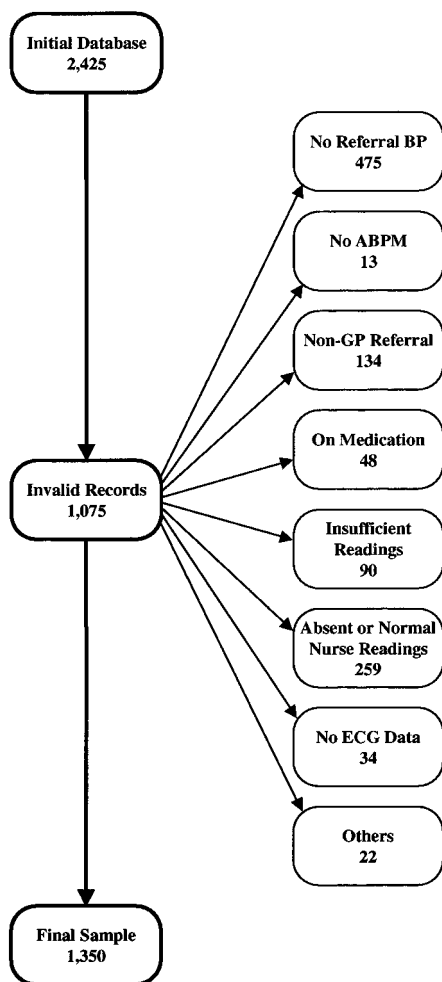
TABLE 2.   Definitions of WCH According to ABPM Measurement Parameters

	Definitions of WCH
Classic definition	• Clinic BP, SBP≥140 or DBP≥90
WCH-C	• Mean Daytime BP, SBP<135 and DBP<85
First reading WCH	• First ABPM reading, SBP≥140 or DBP≥90
WCH-FR	• Mean Daytime BP, SBP<135 and DBP<85
First hour WCH	• Mean of first hour of ABPM, SBP≥140 or DBP≥90
WCH-FH	• Mean Daytime BP, SBP<135 and DBP<85
First hour maximum WCH	• Maximum pressure in first hour of ABPM, SBP≥140 or DBP≥90
WCH-FH$_{max}$	• Mean Daytime BP, SBP<135 and DBP<85
Last reading WCH	• Final reading on ABPM, SBP≥140 or DBP≥90
WCH-LR	• Mean Daytime BP, SBP<135 and DBP<85
Last hour WCH	• Mean of last hour of ABPM, SBP≥140 or DBP≥90
WCH-LH	• Mean Daytime BP, SBP<135 and DBP<85
Last hour maximum WCH	• Maximum pressure in last hour of ABPM, SBP≥140 or DBP≥90
WCH-LH$_{max}$	• Mean Daytime BP, SBP<135 and DBP<85
Ambulatory WCH	• Maximum pressure in first or last hour of ABPM, SBP≥140 or DBP≥90
WCH-A	• Mean Daytime BP, SBP<135 and DBP<85

BP values are given in mm Hg.

data for the study population. On the basis of physician BPs, 148 (11.0%) patients fulfilled the classic definition for white coat hypertension (WCH-C), according to the definitions set out in Table 2.

First ABPM Readings as Markers for WCH
Table 4 shows that a total of 74 (5.5%) patients were categorized as having first reading WCH (WCH-FR). The agreement between WCH-FR and WCH-C was good (κ=0.64), although 50% of WCH-C patients were not identified as WCH-FR. Measurement of first hour WCH (WCH-FH) identified 88 (6.5%) patients in this population. The agreement between WCH-FH and WCH-C was very good

(κ=0.75). Because WCH-FH could conceivably miss the white coat effect due to averaging of a high value with a low value, the highest pressure in the first hour (WCH-FH$_{max}$) was then examined. WCH-FH$_{max}$ identified 115 (8.5%) patients from the population. The agreement between WCH-FH$_{max}$ and WCH-C was excellent (κ=0.86).

Last ABPM Readings as Markers for WCH
Table 4 shows that a total of 60 (4.4%) patients were identified as having last reading WCH (WCH-LR). Agreement for WCH-LR and WCH-C was modest (κ=0.55). Only 33 (2.4%) patients had last hour WCH (WCH-LH), with the poor agreement between WCH-LH and WCH-C (κ=0.34). Finally, the maximum pressure recorded in the last hour (WCH-LH$_{max}$) was also examined as a marker for WCH. This identified 82 (6.1%) patients in the population. Agreement between WCH-LH$_{max}$ and WCH-C was better (κ=0.69).

Combination of WCH- FH$_{max}$ and WCH-LH$_{max}$
WCH- FH$_{max}$ and WCH-LH$_{max}$ were combined in an inclusive relationship to optimize agreement between WCH-C and ABPM parameters of WCH (Table 4). This parameter, called ambulatory WCH (WCH-A), identified 126 (9.3%) patients in the population, and had an excellent agreement with WCH-C(κ=0.91) (P<0.0001).

Clinical Differences Between WCH-C With and Without WCH-A
There were subjects with WCH-A but without WCH-C. When the physician referral BP was compared to BPs of WCH-C patients who were and were not identified by WCH-A, SBPs were significantly higher in those with WCH-A versus those without WCH-A (Table 5). DBP did not differ significantly. Comparisons of ABPM mean daytime

TABLE 3.   Clinical Data and BP for Study Population

Parameter	Mean	SD
Age, y	50.9	12.4
Referral physician SBP	178.4	23.7
Referral physician DBP	105.5	12.0
Nurse SBP	168.2	22.6
Nurse DBP	98.1	12.1
ABPM first hour SBP	160.4	20.7
ABPM first hour DBP	98.9	12.7
ABPM last hour SBP	153.8	20.6
ABPM last hour DBP	94.0	13.8
Daytime SBP	151.6	17.7
Daytime DBP	92.8	11.8
Night-time SBP	131.0	18.5
Night-time DBP	77.2	12.2
Gender, %	56.6 ♀	43.4 ♂

BP values are given in mm Hg.

TABLE 4. 2×2 Tables Showing Relationship Between First (top), Last (middle), and Combined First and Last (bottom) Hour Parameters of WCH and WCH Diagnosed by Classical Methodology

		WCH-FR			WCH-FH			WCH-FH$_{max}$		
		No	Yes	Total	No	Yes	Total	No	Yes	Total
WCH-C	No	1202	0	1202	1202	0	1202	1202	0	1202
	Yes	74	74	148	60	88	148	33	115	148
	Total	1276	74	1350	1262	88	1350	1235	115	1350

$\kappa=0.64$, p<0.0001 $\kappa=0.72$, p<0.0001 $\kappa=0.86$, p<0.0001

P (WCH-FR|WCH-C)=0.50 P (WCH-FH|WCH-C)=0.59 P (WCH-FH$_{max}$|WCH-C)=0.78

		WCH-LR			WCH-LH			WCH-LH$_{max}$		
		No	Yes	Total	No	Yes	Total	No	Yes	Total
WCH-C	No	1202	0	1202	1202	0	1202	1202	0	1202
	Yes	88	60	148	115	33	148	66	82	148
	Total	1290	60	1350	1317	33	1350	1268	82	1350

$\kappa=0.55$, p<0.0001 $\kappa=0.34$, p<0.001 $\kappa=0.69$, p<0.0001

P (WCH-LR|WCH-C)=0.41 P (WCH-LH|WCH-C)=0.22 P (WCH-LH$_{max}$|WCH-C)=0.55

		WCH-A		
		No	Yes	Total
WCH-C	No	1202	0	1202
	Yes	22	126	148
	Total	1224	126	1350

$\kappa=0.91$, p<0.0001

P (WCH-A|WCH-C)=0.85

For each definition, a patient can only belong to one of three groups:
- Hypertensive   (no, no)
- WCH by clinic BP only   (yes, no)
- WCH confirmed by ABPM   (yes, yes)

The κ applies to the full referred population. Although it may be slightly higher than it would be for a general population, where WCH by ABPM but not WCH-C may be greater than 0, it more accurately reflects the population who will be required to wear ABPMs.

The probability of having been diagnosed as WCH by ABPM given that WCH-C has already been observed is also presented.

and nighttime pressures showed significantly higher daytime and nighttime systolic and diastolic mean pressures in patients with WCH-A versus those without WCH-A. Age was also significantly greater in the former versus the latter. Height and weight tended to be higher in WCH-A patients, but not significantly so.

TABLE 5. Comparisons of Clinical Variables, ECG Data and BP Variables in Patients With WCH-C, Between Those Also Positive for WCH-A, and Those Negative for WCH-A

Parameter	WCH-A (n=126)	Not WCH-A (n=22)	P
Age, y	49.8±13.7	40.7±12.0	0.004
Sex, % male/female	47/79	4/18	0.08
Referral SBP	172.7±21.1	160.4±17.3	0.011
Referral DBP	102.6±11.3	98.3±9.6	0.09
Daytime SBP	127.2±5.9	121.6±5.5	0.001
Daytime DBP	77.7±4.9	74.3±5.9	0.003
Night-time SBP	114.0±11.0	106.1±9.0	0.002
Night-time DBP	66.9±8.1	61.1±6.1	0.002
Height, cm	165.9±8.9	163.3±9.3	0.20
Weight, kg	79.1±17.3	73.3±16.2	0.15
V_1+V_5, mV	21.3±7.5	18.1±6.3	0.038
V_1+V_6, mV	19.4±6.8	17.2±5.9	0.131

Values for daytime and night time are ABPM mean pressures.
BP values are given in mm Hg.

To determine independent predictors of WCH-A, a logistic regression model was fitted to the data with WCH-A as the dependent variable, age, height, weight, and daytime and nighttime SBP and DBP as independent variables, and gender as a covariate. Age ($\beta=0.06$, $R=0.26$, $P=0.001$), daytime SBP ($\beta=0.12$, $R=0.22$, $P=0.0047$), and daytime DBP ($\beta=0.12$, $R=0.17$, $P=0.019$) remained independent predictors of WCH-A.

ECG voltages for left ventricular mass, namely V_1+V_5 summation, were significantly greater in WCH-A patients than non–WCH-A patients (21.3±7.5 mV versus 18.1±6.3 mV, respectively; $P<0.038$). However, on multiple regression modeling with V_1+V_5 summation as the dependent variable, WCH-A as a predictor of left ventricular voltage was not independently predictive.

Discussion

WCH is a relatively common finding in patients with elevated BP. The specific numerical definitions vary, but the essential component of the diagnosis is an elevated clinic BP above accepted normal levels, in association with a normal ambulatory BP profile. A variety of normal values are used for ambulatory BP monitoring[14] and, as a result, the proportion of any given population diagnosed as having white coat hypertension has varied widely in the literature.[15]

Our experience of ambulatory measurement has been that it is not entirely free from the white coat effect. This has been

suggested by previous investigators.[16] Specifically, the first or final measurements may be elevated above the mean value for the day. This raises the question of whether these parameters may be useful as markers for the presence of the white coat phenomenon, and, indeed, whether they might identify a separate substratum of patients.

Our data, taken from a large cohort of unmedicated hypertensive patients referred for ambulatory monitoring, show that certain ABPM derived measurements agree well with the traditional methodology of categorization of white coat syndrome. Indeed, it could be suggested that the finding of an elevated reading in the first or last hour of measurement above 140 mm Hg systolic or 90 mm Hg diastolic, when the ambulatory daytime means are normal, is diagnostic of white coat hypertension. The agreement between this methodology and traditional categorization of WCH is not perfect, however, so we propose the term "ambulatory white coat hypertension" as an appropriate label for this finding.

What of the 21.5% of WCH-C patients not identified by WCH-A? Does WCH-A identify a different stratum of true white coat hypertensive patients? We found that there is a large difference in the measured clinic referral pressure between patients who are WCH-A and those who are WCH-C only, with the former having significantly higher pressures. Furthermore, the WCH-A group was older and exhibited significantly higher daytime and nighttime SBPs and DBPs. This suggests that WCH-A identifies a very different stratum of white coat hypertensive patients and identifies patients with more severe white coat hypertension.

The literature remains inconclusive on the subject of whether white coat hypertension carries a pathological risk. Studies for[17–22] and against[2,23–25] this hypothesis have been propounded. The truth most likely lies in the middle, with the risk associated with white coat hypertension substantially less than the risk associated with sustained hypertension, but greater than the risk of true normotensive patients. A methodology that identifies a higher risk white coat group, which WCH-A may well do, would therefore be of significant value in the context of follow-up for this group of patients. The voltage summation of $V_1 + V_5$ for left ventricular mass was higher in our patients with WCH-A than in those with WCH-C only. This reflected the higher BP in these patients, and a difference in body habitus. The definitive statement on this would require a longitudinal outcome study, with WCH-C and WCH-A analyzed as prognostic variables.

A number of caveats need to be considered in interpreting this data. First, although it is reasonable to assume that the stresses that give rise to white coat hypertension might carry over to the first hour of monitoring (when the monitor is applied in a hospital setting), it is perhaps less obvious that these factors would recur in the last hour of monitoring. It was unfortunately not possible, in this study population, to determine which patients returned to the hospital to have their monitors removed (other than to state that it would have been the great majority) and which patients removed the monitors themselves. Therefore, it is possible that the stress of revisiting the hospital, which presumably gave rise to high end pressures on the ABPM, was absent in an undetermined number of our patients. This suggests that if all patients returned to the hospital for removal of their monitors, the agreement between WCH-C and WCH-A would have been higher still. Alternatively, it may be that the approach of the end of the monitoring session was perceived as a stressor in itself, independent of the environment in which it was removed. Second, an obvious choice at the outset of this study was to approach it with a view toward determining the sensitivity and specificity of the ABPM parameters for diagnosis of WCH-C. This, however, involved ascribing the status of "gold standard" to the WCH-C methodology. We felt that this was inappropriate, because the spirit of the definition of white coat hypertension is what is important (measurement of environment-related hypertension with normal average pressures during daily life), rather than a definition strictly involving clinic measurement. Therefore, we took the approach of measuring agreement between 2 potentially complimentary measurement modalities. Finally, there have been concerns expressed over the repeatability of classic white coat hypertension.[26] The reproducibility of WCH-A as defined here has not been formally tested and, thus, also requires formal prospective study.

In conclusion, we have shown that the ABPM can completely and sufficiently diagnose the white coat phenomenon independently of clinic measurement, and we suggest that WCH-A be adopted as a marker of the presence of the white coat syndrome. Furthermore, we have shown that WCH-A identifies a white coat hypertensive subgroup with significantly higher pressures and we speculate that it may stratify patients with white coat hypertension into those who are at very low risk and those who may require more intensive follow-up. Manufacturers of ABPM devices, those who use ABPMs in research, and anybody who provides or uses software for ABPM analysis should allow for this phenomenon, both in the analysis of separate statistics and in the calculation of mean daytime values.

Acknowledgments

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