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Relationship between Clinic and Ambulatory Blood Pressure Measurements in Children

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Abstract: Decision making on diagnosis of hypertension is important to clinicians, patients and general public. We analyzed the agreement between clinic blood pressure (BP) measurements (individual or in combination) and ambulatory wake BP in the diagnosis of hypertension in children. In this study, three sequential clinic BP measurements were performed at the initiation of the 24-hour ambulatory BP monitoring (ABPM) using the identical monitor for both clinic and ambulatory measurements. Ninety patients were reviewed. Pearson Correlation coefficient between clinic BP (individual or in combination) and wake ambulatory BP ranged from 0.81 to 0.85 for SBP and 0.52 to 0.60 for DBP. Multiple regression models showed no improvement using the mean of multiple versus single clinic BP measurements. We also tried principal component method that formed an optimal combination of the clinic measurements. The first principal component accounted about 95% of the total variation, but there was little improvement of the regression model between the wake ambulatory and the first principal component of the three repeated clinic measurements. Our results suggest that assessment for hypertension in children by clinic BP alone is often unreliable and is not improved by multiple BP measurements on a single occasion.

Key words: Ambulatory blood pressure, child, decision making, hypertension, regression.

1. Introduction

One of the most challenging aspects of evaluating and managing patients with hypertension is the interpretation of casual blood pressure (BP) measurements made in the clinic setting. Casual BP is defined in this article as a brief snapshot of the entire 24-hour circadian BP pattern. Studies of adults have demonstrated that these measurements are often unreliable and poorly reflective of patients' BP over a 24-hour period (Mansoor and White 1994, Modesti *et al.* 1994). In

addition, some patients may manifest a transient, stress response when BP is measured in the presence of a medical professional (i.e. White Coat Hypertension). The presence of white coat hypertension (WCH) or white coat effect may lead to overdiagnosis of hypertension or overestimation of the degree of BP elevation in a hypertensive patient (Pickering *et al.* 1999). Although 24-hour ambulatory BP monitoring (ABPM) improves the accuracy of BP assessment, it is impractical to perform ABPM at every juncture in a patient's evaluation and management. Thus, all physicians must rely to some extent on casual clinic-based BP measurements for clinical decision-making. To increase the accuracy of casual BP assessment, the sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-VI) recommends an average of two or more BP measures at each visit (NIH 1997). However, a recent study of adults of BP measurement protocols found 98% agreement and 99% sensitivity for the 2nd reading alone relative to the average of the 2nd and 3rd reading (Huang and Morisky 1999).

The challenge of accurate assessment of BP is no less important in children for whom the risk factor status of cardiovascular disease is approaching epidemic proportions (Daniels 1999). Recent studies of blood pressure screening in school-aged children have shown higher SBP values and a higher prevalence of hypertension than previously reported (Luepker *et al.* 1999). The Task Force on High Blood Pressure Control in Children and Adolescents recommends using the average of two BP measurements at each visit to evaluate for hypertension (NHLBI 1987). However, even among children with elevated casual BP documented on multiple occasions, a recent study found a prevalence of WCH of 56% in children with documented clinic hypertension when BP was assessed by ABPM (Sorof and Portman 2000). No studies in children have documented the reliability of either the JNC-VI or Task Force protocols by comparing clinic BP measurements with subsequent 24-hour ABPM in terms of agreement with actual BP values or determination of hypertension status. To determine whether multiple clinic BP measurements improve the reliability of clinic BP relative to ambulatory BP, we reviewed the records of children and adolescents who underwent three clinic BP measurements immediately followed by 24-hour ABPM.

2. Data Collection and Methodology

The records of children who underwent ABPM for BP assessment were reviewed. Demographic data collected on patients included age at evaluation, gender, race, height, weight, and body mass index (BMI) defined as the weight in kilograms divided by square meters of the height. Size-appropriate BP cuffs were placed on the non-dominant arm. Blood pressure measurements were then performed while seated after 5 minutes of rest. Clinic BP values were obtained

by performing three sequential BP measurements (BP1, BP2, and BP3) at the initiation of the 24-hour monitoring by manual activation of the ABPM oscillometric monitors (Spacelabs 90207 or 90217, Seattle, WA). These monitors have been previously validated to within 4% for SBP and 1% for DBP in children by comparison with auscultatory measurements by trained observers (Portman, Yetman and West 1991). Twenty-four hour ABPM was then initiated using the same BP monitor as was used for the clinic BP measurement for each individual patient. BP was measured every 20 minutes for 24 hours. If BP was unable to be measured at a scheduled time, one additional measurement was automatically attempted 3 minutes later. To be included in the analysis, a minimum of one successful BP measurement each hour for the entire 24-hour period was required. Wake and sleep periods were determined by actigraphs (wristwatch-sized accelerometers that detect motion and determine periods of sleep based on decreased frequency and amplitude of motion).

Hypertension status was determined separately for clinic and ambulatory BP measurements. Clinic hypertension status was determined for each individual clinic BP measurement (BP1, BP2 and BP3), the mean of BP1 and BP2 (BP12), the mean of the BP2 and BP3 (BP23), and the mean of all 3 measurements (BP123). Clinic hypertension was defined as either SBP or DBP above the gender, age, and height-specific 95th percentile from the most recent Task Force Update (NHLBI 1996). Ambulatory hypertension was defined as an average wake SBP or DBP above the 95th percentile value from the Task Force Update (NHLBI 1996) . White coat hypertension was defined as hypertension by clinic BP criteria with normotension by ambulatory BP criteria.

Differences between individual clinic BP measurements were assessed by ANOVA and between clinic BP and ambulatory BP measurements were assessed by pairwise t-tests. The relationships between clinic and ambulatory BP parameters were assessed by Pearson correlation coefficient. The percent error of clinic relative to wake ambulatory BP was calculated as the absolute value of the difference between clinic and ambulatory wake BP divided by ambulatory wake BP multiplied by 100%. Multiple regression analysis combining with the principal component analysis (Anderson 1984) was used to determine the combination of independent factors that were most predictive of ambulatory BP. Differences in the prevalence of WCH among different patient subgroups were assessed by either Chi-squared test or Fisher's exact test. A p value of less than 0.05 was considered the threshold for statistical significance.

3. Characteristics of the Data

Ninety pediatric patients were included in the analysis. Sixty-one patients were undergoing first evaluation for persistently elevated casual BP, 12 patients

Table 1: Demographic, anthropometric, and blood pressure data for all subjects

		Mean	SD
Age and Anthropometrics			
	Age (yrs)	11.4	3.8
	Weight (kg)	59.9	30.0
	Height (cm)	149.7	24.7
	BMI (kg/m^2)	24.9	7.5
Clinic BP (mmHg)			
	SBP1	125.2	18.5
	SBP2	124.6	17.5
	SBP3	124.7	17.9
	DBP1	76.4	13.4
	DBP2	75.1	11.5
	DBP3	74.7	11.8
Ambulatory BP (mmHg)			
	Number of Readings	57	11
	24-hour SBP	119	11
	Wake SBP	124	13
	Sleep SBP	110	10
	24-hour DBP	69	7
	Wake DBP	74	8
	Sleep DBP	60	8

were undergoing evaluation for efficacy of antihypertensive medications, and 17 patients were normotensive volunteers. The mean duration of monitoring was 23.7 hours with standard deviation 2, the mean success rate was 64% with standard deviation 16%, and the mean number of successful readings was 57 with standard deviation 11. Demographic, anthropometric, and BP data for all patients are shown in Table 1.

The histograms of the casual clinic blood pressures are presented in Figure 1 and the histograms of the average ambulatory blood pressure are given in Figure 2.

From Figures 1 and 2, one can see that the distributions of the data are not far from a normally distributed random variable except a few outliers.

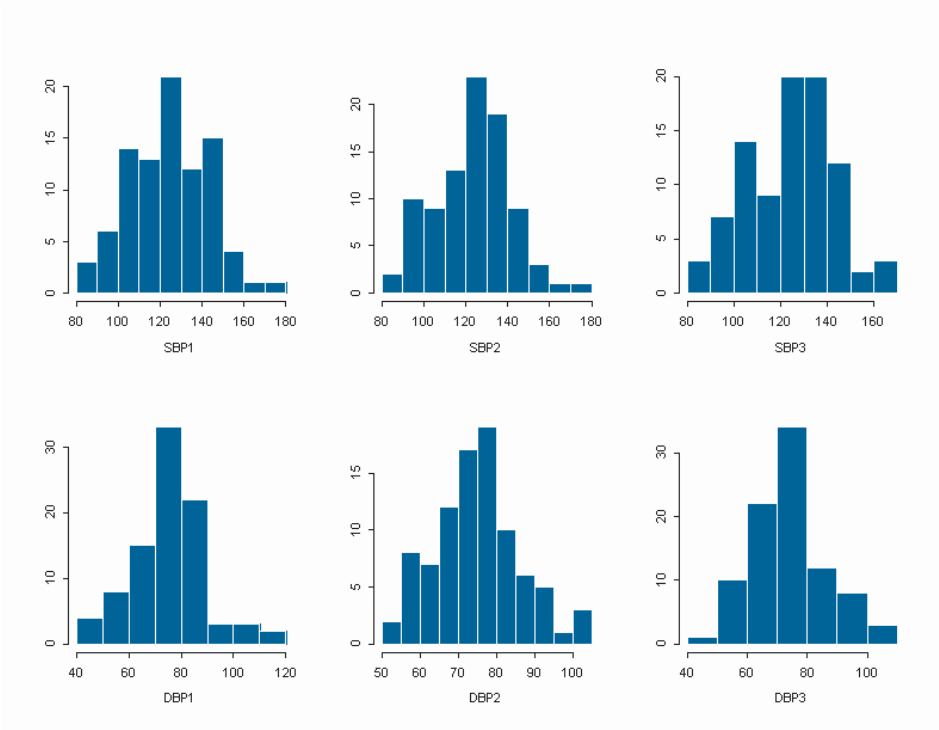

Figure 1: Histogram of the clinic BP measurements. SBP1=First clinic SBP measurement, SBP2=Second clinic SBP measurement, SBP3=Third clinic SBP measurement, DBP1=First clinic DBP measurement, DBP2=Second clinic DBP measurement, DBP3=Third clinic DBP measurement.

4. Correlation Coefficient and Regression Analysis

The strength of the relationship between clinic and wake ambulatory BP values was determined by calculation of Pearson correlation coefficients. Wake BP was chosen as the ambulatory hemodynamic variable that would most closely approximate the clinic BP measurements. All clinic BP values for both SBP and DBP were significantly correlated with wake ambulatory BP. The correlation coefficients for clinic SBP and wake ambulatory BP ranged from 0.81 to 0.85. The highest correlation coefficient was for SBP123 ($r = 0.85, p < 0.0001, d.f. = 88$). The correlation coefficients for DBP ranged from 0.52 to 0.60. The highest coefficient was for DBP123 ($r = 0.60, p < 0.0001, d.f. = 88$). Combined clinic BP measurements did not demonstrate significantly higher correlation with ambulatory BP than individual measurements. Overall, the correlation coefficient between clinic and ambulatory BP was higher for SBP than for DBP. The Pearson correlation coefficient between the wake ambulatory SBP and the first principal

component of the clinic SBP measurements was 0.83 ($p < 0.0001, d.f. = 88$). Although the first principal component accounted about 95% of the variation of the measurements, it did not improve the predictability of the clinic SBP measurements for the wake ambulatory SBP.

Multiple regression analysis between ambulatory and clinic BP was performed. All individual clinic SBP and DBP values were significant independent factors for the determination of wake ambulatory BP. Age was a significant independent factor for wake ambulatory SBP, but not for wake DBP. Patient type (hypertensive, hypertensive on medication, or normotensive), gender and race were not significant variables in the regression models. Linear regression revealed that the model for SBP that yielded the highest R^2 with the two independent variables was age and SBP123 ($r = 0.72, p < 0.001, d.f. = 88$). The model that yielded the highest R^2 with the one independent variable (age was not significant in this model) for DBP was for DBP123 ($r = 0.41, p < 0.001, d.f. = 88$). None of the models for the various combinations of clinic BP differed significantly from each other. The details of the model fitting are given in Table 2.

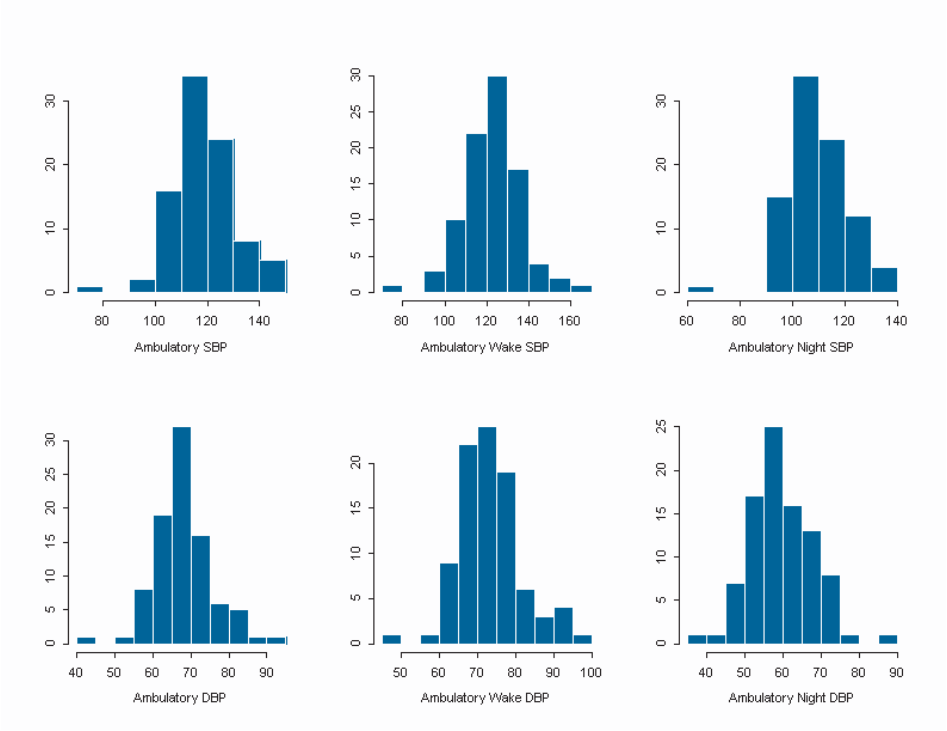

Figure 2. Histogram of the ambulatory BP measurements.

Table 2: Multiple regression models for ambulatory wake BP vs. clinic BP

	α	β_1	β_2	R^2	d.f.	p-value
SBP						
SBP1 & Age	50.94	0.51	0.80	0.71	87	< 0.0001
SBP2 & Age	49.09	0.54	0.72	0.69	87	< 0.0001
SBP3 & Age	50.44	0.53	0.61	0.69	87	< 0.0001
SBP12 & Age	47.39	0.55	0.73	0.72	87	< 0.0001
SBP23 & Age	47.64	0.55	0.64	0.71	87	< 0.0001
SBP123 & Age	46.70	0.56	0.66	0.72	87	< 0.0001
DBP						
DBP1	45.24	0.37		0.39	88	< 0.0001
DBP2	45.16	0.38		0.30	88	< 0.0001
DBP3	42.80	0.41		0.38	88	< 0.0001
DBP12	42.88	0.41		0.37	88	< 0.0001
DBP23	40.58	0.44		0.37	88	< 0.0001
DBP123	40.40	0.44		0.40	88	< 0.0001

SBP Model(s): Ambulatory wake SBP $= a +$ β_1(Clinic BP) $+ \beta_2$(Age)
DBP Model(s): Ambulatory wake DBP $= \alpha +$ β_1(Clinic BP)

To determine the actual numerical agreement between clinic and ambulatory BP values, the percent error of the clinic BP values was determined. For each patient, two percent errors were computed, one between ambulatory BP and SBP2 and another between ambulatory BP and the mean of the first two casual clinic BP measurements. The mean percent error of clinic SBP relative to the wake ambulatory SBP ranged from 6.7% to 7.4%. Pairwise t-test showed that the percent error did not differ for SBP2 alone compared to the mean of SBP1 and SBP2 ($p = NS, d.f. = 89$).

Figure 3 shows the mean percent error of SBP2 relative to wake ambulatory SBP. Similarly, the percent error of clinic DBP relative to the mean wake DBP ranged from 10.5% to 12.5%. Pairwise t-test showed that the percent error did not differ for DBP2 alone compared to the mean of DBP1 and DBP2 ($p = NS, d.f. = 89$). Figure 4 shows the percent error of DBP2 relative to wake ambulatory DBP. Overall, the percent error for SBP was significantly lower than for DBP ($p < 0.0001, d.f. = 89$).

To determine the relative agreement of diagnosis of hypertension status between clinic and ambulatory BP, the group of patients undergoing evaluation for persistently elevated BP was analyzed separately. For individual clinic BP mea-

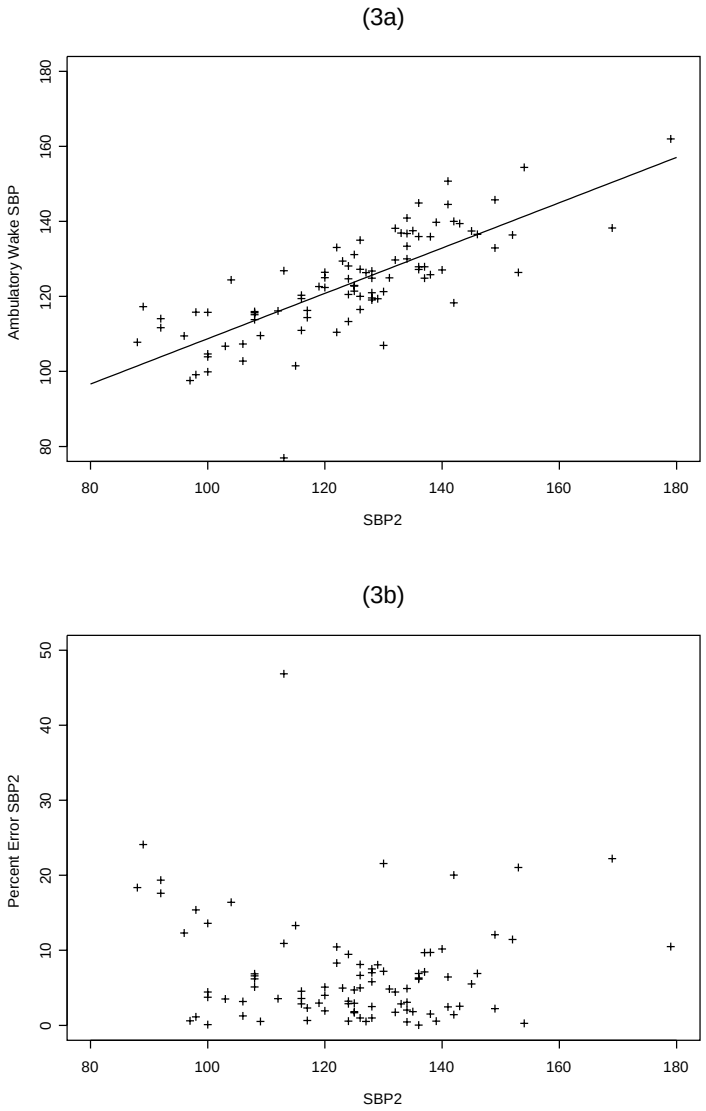

Figure 3: Correlation and percent error of ambulatory wake SBP relative to SBP2
3a. Solid line shows the regression line between mean ambulatory wake SBP and SBP2
SBP2=Second clinic SBP measurement Ambulatory Wake SBP=Mean ambulatory BP measurements during wake period
3b. Percent error of SBP2 relative to mean ambulatory wake SBP
Percent error=$|\text{SBP2} - \text{Wake SBP}|/\text{Wake SBP} \times 100\%$

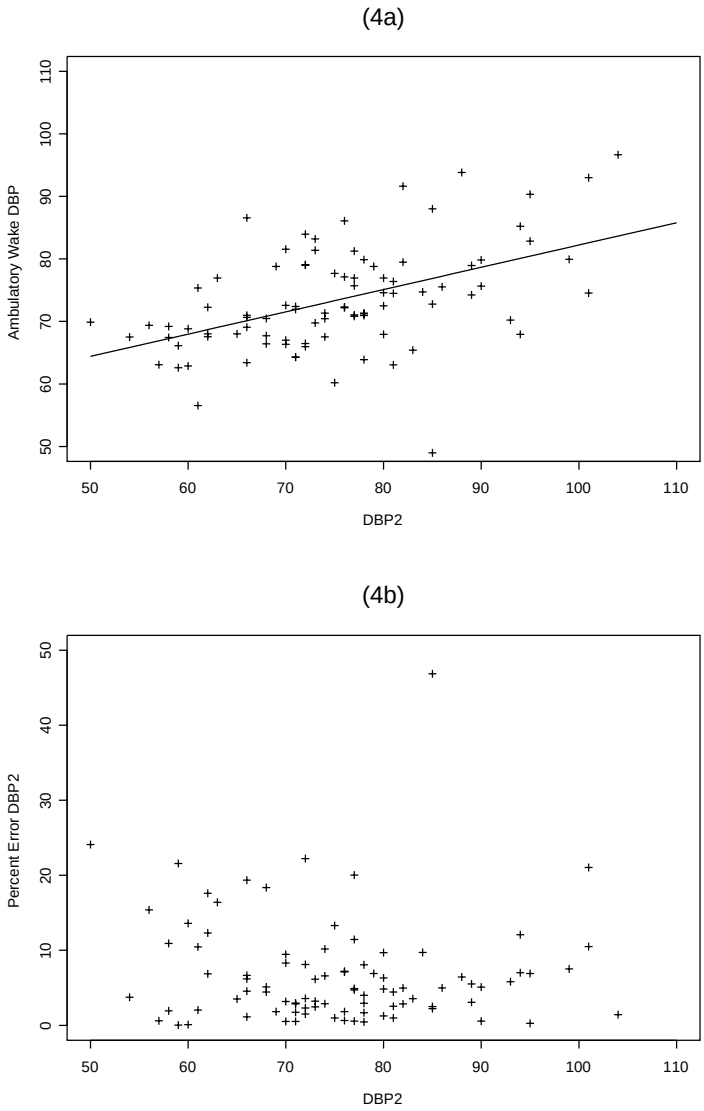

Figure 4: Correlation and percent error of ambulatory wake DBP relative to DBP2.
4a. Solid line shows the regression line between mean ambulatory wake DBP and DBP2
DBP2=Second clinic DBP measurement
Ambulatory Wake DBP=Mean of ambulatory BP measurements during wake period
4b. Percent error of DBP2 relative to mean ambulatory wake DBP Percent error=|DBP2-Wake DBP|/Wake DBP x 100%

surements, the prevalence of clinic hypertension decreased from 84% (BP1) to 79% (BP2) to 77% (BP3). For the mean of all three clinic BP readings (BP123), the prevalence of clinic hypertension was 77% (47/61). The prevalence of WCH in this group was 28% (13/47). The prevalence of WCH did not significantly differ when each clinic BP measurement was used alone to determine clinic hypertension status, nor was there a difference in the prevalence of WCH by gender or race. The odds ratio of clinic hypertension status correctly predicting ambulatory hypertension status was 10.7 (95-th % C.I. 3.0 – 37.8).

5. Discussion of the Results

Clinic BP measurements have been used extensively and successfully to predict cardiovascular risk in adults. However, for a given individual the clinic measurements may be prone to overestimation of the usual BP due in part to transient stress-induced BP elevation. Recent studies in children have reported a prevalence of WCH of 44-88% (Sorof and Portman 2000), suggesting that clinic BP measurements often overestimate the usual BP in a non-medical setting. To improve the reliability of hypertension assessment, the pediatric advisory committee for the evaluation of BP in children has advocated combining multiple BP measurements at each visit. Specifically, the Update on the 1987 Task Force on High Blood Pressure in Children and Adolescents recommends that BP be recorded at least twice on each occasion and the average used to estimate BP (NHLBI 1987). This recommendation has not been validated by comparing clinic BP measurements with the results of ambulatory BP monitoring to determine whether combining multiple measurements improves reliability compared to single BP measurements.

The current study confirms the results from previous studies showing the poor reliability of clinic BP to accurately diagnose hypertension in children with 28% WCH. In addition, it is the first study in children to show that multiple clinic BP measurements at a single visit do not improve the reliability of casual BP assessment relative to ambulatory BP since there is no statistical significant difference among 84% (51/61), 79% (48/61) and 77% (47/61) ($\chi^2 = 0.8802, p = 0.6438, d.f. = 2$). One of the strengths of this study is that ABPM was performed immediately following the clinic BP measurements, thereby minimizing the confounding effect of normal BP variability over time. An additional strength is that an identical oscillometric monitor was used for both clinic and ambulatory BP measurements, thereby avoiding the confounding effect of systematic differences in methodology between auscultatory and oscillometric BP measurements. Using this approach, the results from the current study demonstrated that clinic BP measurements were only moderately predictive of wake ambulatory BP with no significant improvement by the use of multiple

measurements. Furthermore, the likelihood of miscategorization of hypertension status was not reduced by additional clinic measurements. Thus, multiple clinic measurements neither improved the correlation with ambulatory BP values nor the concordance of diagnosis of hypertension.

The current study is consistent with a previous study of hypertensive and normotensive children showing that casual and ambulatory wake BP values are significantly correlated, with the correlation higher for SBP than for DBP (Nishibata *et al.* 1995). However, this method for assessing relative agreement may be misleading. Both the current and previous study found that the casual BP measurements were significantly higher than the ambulatory measurements. Systematic differences between two methods of measuring the same parameter may result in excellent correlation but poor agreement. For this reason, the relationship between clinic and ambulatory BP is better represented by the absolute percent error that, in the current study, was found to be approximately 6-7% for SBP and 10-12% for DBP. Thus, clinic BP measurements consistently overestimated ambulatory BP, leading to a higher prevalence of hypertension by clinic BP criteria.

The results from the current study are also consistent with a previous study of adults comparing the mean of the 2-nd and 3-rd measurement with the 2-nd measurement alone (Huang and Morisky 1999). In the previous study, it was found that stability of sequential BP measurements was established by the 2-nd measurement, and that the sensitivity and false-negative rate of the 2-nd measurement relative to the mean of the 2-nd and 3-rd was 98.73% and 0.43%, respectively. In the current study, SBP2 tended to be the lowest of the three sequential measurements, and DBP2 was significantly lower than DBP1. In addition, the diagnosis of hypertension by clinic BP criteria was not improved by multiple measurements. The prevalence of WCH was 29% based on clinic BP2 and 28% based on BP123. Relative to the recommended protocol of the Task Force, the current study suggests that casual BP assessment is as accurate by consideration of only a single clinic BP measurement as for the combination of three clinic measurements.

Although a diagnosis of WCH in children may be somewhat reassuring in the short-term, WCH may be a pre-hypertensive state that progresses to persistent hypertension in some children with increasing age. WCH may be a more general manifestation of the phenomenon of enhanced cardiovascular response to stress, which has been found to predict higher future resting blood pressure, persistent hypertension, and structural cardiac changes (Del Rosario *et al.* 1998, Kapuku *et al.* 1999). Thus, while the diagnosis of WCH by ABPM may obviate the need for extensive diagnostic evaluation for secondary causes of hypertension in children, it should not be considered an indication that future assessment is unnecessary

6. Concluding Remarks

The conclusions that may be drawn from the current study are limited by several factors. The use of ABPM monitors to measure clinic BP is not typical and may therefore not entirely mimic clinical practice. Furthermore, the Task Force percentiles for defining pediatric hypertension are based exclusively on auscultatory BP measurements. However, several studies have verified the accuracy and reliability of oscillometric compared to auscultatory BP techniques in adults (Brinton *et al.* 1998, Baumgart and Kamp 1998), and the specific model of monitors used in this study (Spacelabs 90217) has been tested for compliance with the Association for the Advancement of Medical Instrumentation's standard and a modification of the British Hypertension Society (BHS) protocol (Baumgart and Kamp 1998) In addition, the oscillometric monitors used in this study have been validated in children and found on average to overestimate SBP by only 4% and DBP by only 0.3% by comparison with simultaneous auscultatory mercury manometer measurements (Portman, Yetman and West 1991). A further limitation is that the current study addresses only within-visit reliability and not the issue of sequential measurements at different time points. Several studies of children have found that multiple casual BP measurements over time increase the reliability of hypertension assessment and the prediction of future hypertension status (Gillman *et al.* 1991, Rosner *et al.* 1987). Repeated ABPM might similarly be expected to result in normalization of ambulatory BP by simple regression to the population mean. However, it has been reported in children that ABPM results are reproducible when subsequent repeat monitoring is performed (Lurbe *et al.* 1993). Finally, this study evaluates only wake ambulatory BP. Disturbances of 24-hour BP patterns, such as failure to have the normal sleep decline in BP, may represent independent cardiovascular risk factors that are not addressed in this study.

In summary, the current study confirms that identification of hypertension status in children by clinic BP alone is often unreliable even with multiple measurements. However, the results do demonstrate that clinic BP is a useful tool for initial hypertension screening. Clinic BP measurements, either alone or in combination, were significantly correlated with wake ambulatory BP and the odds ratio for identification of ambulatory hypertension status by clinic hypertension status was greater than 10. Thus, when ABPM is not feasible, such as in the setting of BP screening programs or for routine BP assessment, the 2-nd of two BP measurements alone appears to be as reliable as the average of three measurements. Nonetheless, the percent error of the clinic values ranged from 6-12% and the percentage of patients with persistent clinic hypertension and ambulatory normotension ranged from 25-30%. The Task Force recommendations are

directed primarily at routine assessment of BP that requires serial measurements on different occasions to confirm the diagnosis of hypertension. Regardless of the number of measurements, the diagnosis of hypertension requires persistent BP elevation on multiple occasions. Once persistent clinic BP elevation is established, for the purposes of clinical decision-making ABPM should be performed as part of the routine diagnostic evaluation.

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