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EDITORIAL COMMENTARY

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Utility of ambulatory blood pressure monitoring in children and adolescents

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Abstract Diagnosis of hypertension is critically dependent on accurate blood pressure measurement. "Accurate" refers to carefully following the guidelines for blood pressure measurement laid out for children and adults to minimize observer and subject errors that commonly occur in clinical blood pressure measurement. Accurate blood pressure measurement is more important in children and adolescents as the misdiagnosis of hypertension may have a life-long adverse impact on insurability and employment. Automated blood pressure measurement offers multiple advantages in achieving high-quality blood pressure determinations by reducing observer errors. The most commonly used form of automated blood pressure measurement is 24-h ambulatory blood pressure measurement (ABPM). Information on ABPM in children has grown exponentially over the last decade. Normative data exists for diagnosis of hypertension in children using ABPM including a novel method for determining normal values with the LMS method. There is further information about the utility of different determinants of 24-h blood pressure such as dipping status, morning surge and blood pressure load. ABPM has been able to detect significant differences in blood pressure in many disease states in children including chronic renal failure, polycystic kidney disease, solitary functioning kidney, and after renal transplantation. Increasingly nonambulatory automated blood pressure determinations have been used in management of hypertension in children. Although nonambulatory automated readings lack information about nocturnal blood pressure or blood pressure during daily activity, studies have suggested that home automated blood pressure measurements are a helpful adjunct to the usual office blood pressure reading.

Keywords Ambulatory blood pressure measurement · Hypertension in children · Accurate blood pressure

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Introduction

Blood pressure (BP) measurement in children and adolescents can present a unique challenge to the clinician as interactions among the child, parent and clinician may induce errors in blood pressure measurement. The 1987 Working Group guidelines for blood pressure measurement in children and adolescents [1] outline the correct technique for accurate blood pressure measurement and were not changed in the most recent report in 2004 [2]. It should be noted that the 1987 Report of the Working Group on Blood Pressure Measurement in Children and Adolescents involved two important changes in blood pressure measurement. First it changed the definition of diastolic blood pressure from use of phase 4 Korotkoff sounds to the use of phase 5 as is done in blood pressure measurement in adults. Secondly, this report also expanded the normative tables for blood pressure from the previous report to incorporate the impact of height on normal values for blood pressure measurement. De Man et al. have shown that these normative values for European children are different than those for American children. Pooling information from six European studies (four countries: Germany, France, Denmark, and the Netherlands) showed that the 95th percentile for mean blood pressure was higher by 6 mm Hg for systolic blood pressure (SBP) and 3 mm Hg for diastolic BP (DBP) in both girls and boys [3]. Menghetti and colleagues found that normal values for blood pressure for Italian children differed from both the American data and also from de Man's [4]. Italian children, with respect to the American standards for the 90th and 95th percentiles were 3–8 mm Hg higher for systolic and diastolic blood pressure in both sexes between 5 and 12 years of age and 2–3 mm Hg higher in

older males. Unique to pediatric hypertension, diagnosis of hypertension requires both accurate blood pressure measurement and knowledge of the normal values of blood pressure in the population the clinician is caring for.

Accurate blood pressure determination remains elusive in clinical practice. Unfortunately, it has been demonstrated that primary care physicians [5] or nurses [6] rarely conform to the guidelines when measuring blood pressure in clinical practice. This may be due to failure to train these observers adequately as was noted by Grim and Grim [7] as well as underemphasis of the importance of accurate blood pressure measurement in the literature [8]. Failure to follow the guidelines regarding patient positioning, such as sitting with back supported and feet on the floor [9–11], arm supported at heart level [11], appropriate size cuff applied [12, 13], and use the mean of two or more blood pressure measurements for the diagnosis of hypertension [14], can induce significant errors in blood pressure measurement.

Another important change in blood pressure measurement in children and adults is the movement away from the mercury manometer, based on environmental concerns about mercury contamination from broken manometers [15, 16]. Aneroid sphygmomanometers are a viable alternative, but research has shown that they require careful, frequent calibration and maintenance by biomedical engineers to be accurate [17], services that are not readily available to most practitioners. This has led to an increased interest in the use of automated blood pressure measurement devices, which use the oscillometric technique to measure blood pressure. Briefly the oscillometric technique works as follows: as the cuff is deflated, the sensor in the automated device detects oscillations in the artery, with the point of maximum oscillation correlating well with mean arterial pressure. Systolic and diastolic blood pressures are then calculated using a proprietary algorithm of the slope of rise and fall of the oscillations [18]. Not all of these devices are sufficiently accurate to use for diagnosis and treatment of high blood pressure. For example, Rose and colleagues found that the Dinamap device algorithm had a significant flaw [19]. The device had multiple skipped digits, values for systolic and diastolic blood pressure that the device would never record; making it unsuitable for use in hypertension management. Protocols have been devised to test oscillometric devices, such as the one by the British Hypertension Society [20] and the International Protocol [21], to examine whether these devices have sufficient accuracy to be used in the management of hypertension.

There is an amazing dearth of information about the accuracy of oscillometric blood pressure measurement devices in children. Validation studies of oscillometric devices in children using these protocols have not identified any devices that have passed in children [22, 23]. Attempts at device validation using an alternative protocol [24] demonstrated again the failure of the oscillometric device to perform with sufficient accuracy to be used in hypertensive patients [25]. Wankum's study of a wrist oscillometric device in an intensive care setting in children 12 months to 17 years showed strong correlations with interarterial pressure and oscillometric determinations of SBP (R=0.93), DBP (R=0.93) and mean arterial pressure (MAP) (R=0.94), but no correlations with auscultatory blood pressure were reported [26]. The BpTRU (VSM MedTech, Coquitlam, BC) oscillometric device has been shown to perform well in children [27] in office settings.

The rapid progress in blood pressure measurement and blood pressure measurement device validation is best monitored via the Web site http://www.dableducational.com [28]. Under the leadership of Dr. Eoin O'Brien, this not-for-profit Web site is the most current repository of new evidence in this area. Oscillometric devices and their algorithms are greatly influenced by the underlying arterial stiffness of the subject [29]. Since arterial stiffness changes with age, devices that pass validation testing in adult subjects may not necessarily perform as well in children and adolescents with less stiff arteries than adults. Support for this comes from Lurbe and colleagues. When they looked at the Spacelabs 90207 (Spacelabs Medical, Hawthorne, CA) for reproducibility in children, they observed that in children with narrow auscultatory office pulse pressure there was a marked increase in erroneous measurements with the Spacelab 90207 device. This suggests that the Spacelabs algorithm for blood pressure measurement failed to perform as well in the pediatric population.

The failure to provide validation studies with automated oscillometric blood pressure measurement devices in children has not stopped the development of a large body of research in ambulatory blood pressure measurement (ABPM) in children and adolescents. However, certainly caution must be used in reviewing ABPM data in children due to lack of information about the accuracy of these devices in the pediatric population.

Thus, although not all agree with the movement away from auscultatory blood pressure measurement to use of automated oscillometric devices [30], increasingly they are being relied upon for use in multiple clinical settings. This includes 24-h ambulatory, non-ambulatory automated office and home automated blood pressure measurement.

Ambulatory blood pressure measurement (ABPM)

The current Fourth Working Group Report acknowledges the advance in information about 24-h ABPM and its use in children to diagnose hypertension that has occurred since the 1996 [1] report. It concludes that APBM has a limited role: "ABPM in children and adolescents should be used by experts in the field of pediatric hypertension who are experienced in its use and interpretation" [2]. Table 1 outlines the areas where 24-h APBM has been used in adults, and where data are available now that did not exist at the time of the last comprehensive review of ABPM in this journal [31].

Table 1 Uses of 24-h ABPM

Diagnosis
Hypertension*
White-coat hypertension*
Masked hypertension*
Reproducibility of ABPM *
Special considerations
Autonomic dysfunction*
Treatment response*
Dipping status*
Treatment outcomes
Sleep apnea*
Morning surge

*Data available in children

Diagnosis of hypertension

Adults

Three main studies form the background for the current definition of hypertension and normotension based on 24-h ABPM. Determinations of "normal" ABPM have been done using either the 95th percentile [32], regression analysis linking the patient's office and 24-h ABPM [33] or using outcomes-analysis of 24-h ABPM [34]. All three methods have reached similar conclusions about "normal," which have been incorporated into the JNC VII Guidelines [35] as awake blood pressure less than or equal to 135/85 or less than or equal to 120/75 while asleep [35].

Children

Portman described one of the first large population studies of ABPM in children [36]. He was able to show that 24-h ABPM could be successfully used in the pediatric population. Four large studies [37–40] with subjects from the United States, Spain, Germany, and Taiwan have added important information aiding in the establishment of normal values for ABPM in children by linking ABPM to age and gender as the standard tables do for office blood pressure determinations in the diagnosis of children (Table 2). As seen with office blood pressure, normal values for ABPM rise with age, and values for boys tend to be higher than for girls at the same age. Population differences with APBM, similar to differences reported with causal blood pressure measurement, were also seen with Taiwanese blood pressures tending to be lower at a given age compared to those reported in children of western European descent.

Table 3 shows data from two of the three studies that have indexed ABPM results to age and height to provide further background information to allow ABPM to be used for early diagnosis of hypertension in children and adolescents [41–43]. Values obtained by Soergel in German and Hungarian children using the Spacelabs 90207 look very similar to the data collected by Wasilewski in

Table 2 ABPM values in children and adolescents from the literature

Author	Year	Population	Age (years)	Boys	Girls	Total	Device	Design	Awake ABPM				Comments
									Boys		Girls		
Harshfield	1994 [37]	U.S. (normotensives)	10–18	160	140	300	Space labs 5200, Accutraum 2	Prospective	10–12	13–15	16–18	10–11	13–15	16–18	AA and Caucasian
									115±9/ 67±7	116±11/ 65±6	125±12/ 69±5	112±9/ 65±5	112±8/ 66±7	111±9/ 70±6	
Lurbe	1994 [38]	Spain	6–16	126	115	241	Space labs 90207	Prospective	6–9	10–12	13–16	6–9	10–12	13–16	95% percentile for mean ABPM
									121/71	123/78	124/78	119/71	120/74	125/75	
Reichert	1995 [39]	Germany	9–13	155	139	294	Space labs 90207, Oxford Medilog	Prospective	11–12	12–13		11–12	12–13		Subset analysis, BP indexed to ht/wt
									113±9/ 71 ±8	115±13/ 70±10		113±8/ 70±7	113±9/ 69±9		
Weng	2002 [40]	Taiwan	6–14	64	56	120	BPM AM 200	Prospective	6–8	9–11	12–14	6–8	9–11	12–14	
									110±7/ 74±4	117±5/ 75±4	122±6/ 76±4	109±8/ 72±5	115±8/74±6	120±7/ 75±6	

Table 3 Studies with ABPM results indexed to age and height

Author	Year	Population	Age	Boys	Girls	Total	Device	Design	Awake ABPM						Comment
									Boys			Girls			
									Ht (cm)	50th	95th	Ht (cm)	50th	95th	
Soergel	1997 [41]	Central Europe		639	615	1141	Space labs 90207, Meditech	Prospective	120	112/73	123/85	120	111/72	120/84	Impact of height on ABPM. Different from casual BP
									130	113/73	125/85	130	112/72	124/84	
									140	114/73	127/85	140	114/72	127/84	
									150	115/73	129/85	150	115/73	129/84	
									160	126/78	134/85	160	116/73	131/84	
									170	121/73	135/85	170	118/73	131/84	
									180	130/77	137/85	180	120/74	131/84	
Wasilewski	2004 [43]	Poland	7–17	419	333	852	Quiet Tycos	Prospective	120	107/74	116/78	120	106/70	113/78	
									130	112/74	120/80	130	110/72	119/80	
									140	114/71	124/80	140	114/73	124/80	
									150	118/72	129/82	150	119/74	129/83	
									160	118/74	129/81	160	120/72	131/84	
									>170	125/74	133/84	>170	126/74	132/84	
O'Sullivan	1999 [42]	UK	6–16	452	669	1,121	TM2421	Prospective	Rest 130[a]		Day 160[a]		Night 130[a]		Tables indexed to ht

[a]95th percentile systolic blood pressure

Polish children using the Quiet Tycos ABPM (Welch Allyn Medical Products, Skaneateles Falls, NY). This suggests the normal values for ABPM in children of European descent maybe closer to each other than the normal values reported for casual BP in these populations.

Wuhl et al reported on a novel method, the "LMS" method [44], for calculating reference values for ABPM in healthy children [45]. Similar to the concerns raised by Mancia in adults, simply using the 95th percentile to define hypertension seemed inadequate as Wuhl and colleagues recognized that 24-h ABPM in children had a nonGaussian distribution. In their paper they derived age- and gender-specific estimates of the distribution median (M), coefficient of variation (S), and degree of skewness (L), which were obtained by a maximum likelihood of curve fitness technique. These were then applied to normalize ABPM data to gender and age or height. This should result in the reduction of over- and underdiagnosis of hypertension in children. If this is true, as it seems to be, it greatly enhances the use of ABPM over casual office blood pressure determination, with its many well-identified potentials for error [46], as the tool to diagnose hypertension in children. Accurate diagnosis in children is more important than in adults as the complications of hypertension are strongly related to its longevity; as well, the known social consequences (life- and health-insurance affordability) of an incorrect diagnosis are more significant.

Simple dichotomous cutoff values for ABPM for normal BP versus hypertension may not be sufficient in adults or children. Zachariah and coworkers identified that adults with office BP near the value for hypertension of ≥140/90 mm Hg could have an average 24-h ABPM value that was "normal" and still have a highly variable number of individual readings above normal. They developed the concept of "blood pressure load," defined as the percentage of ABPM readings ≥140 mm Hg for SBP and ≥90 mm Hg for DBP [47]. The importance of this point has been emphasized by subsequent authors who have related blood pressure load to target organ damage [48, 49]. However there has yet to be a consensus as to what is the acceptable limit of blood pressure load, a point that is not currently addressed by any of the hypertension guidelines [35, 50, 51], the last consensus conference on ambulatory blood pressure monitoring [52], or the 2005 Workshop on Blood Pressure Measurement of the European Society of Hypertension [53].

Studies on the effect of blood pressure load as a diagnostic tool in children are limited to three papers. The first, by Sorof [54], looked at the impact of blood pressure load on the diagnosis of white-coat hypertension (WCH; elevated office casual blood pressure with normal 24-h ABPM) in a study of 67 children who had 24-h ABPM done for elevated casual blood pressure over a 2-year period. BP load was defined as abnormal if >25% of readings were above the norm on ABPM. Fifty-one of these children had confirmed hypertension according to Task Force Criteria [1]. The diagnosis of WCH in this population was 53% if Task Force criteria were used, 45% using ABPM data as defined by Soergel [41], and 22%

using ABPM data as defined by Soergel together with BP load of <25%. In addition, elevated blood pressure load was found in 52% (12/23) of patients with mean normal ABPM. Khan reported a retrospective review of 7 years of ambulatory monitoring in a referral population. They found that a blood pressure load of greater than 30% was seen in 89% of these subjects [55]. Koshy et al. extended Khan's look at blood pressure load by examining the agreement between mean ABPM above the 95th percentile and blood pressure load greater than 30% (more than 30% of readings greater than the 95th percentile) in a study of 728 ABPM in subjects less than 19 years of age and 115–184 cm in height [56]. The agreement for daytime SBP and DBP between blood pressure load of 30% and mean ABPM above the 95th percentile was "moderate" at best with kappa coefficients of 0.56 and 0.57, respectively. Nighttime agreement was better with kappa coefficients of 0.70 for SBP and 0.66 for DBP. Maximum agreement occurred with a BP load of 50%.

White-coat hypertension

Adults

ABPM has been the primary tool to identify the deficiencies of office blood pressure determination in the diagnosis of hypertension. ABPM showed that there were patients with white-coat hypertension and more recently patients with masked hypertension (normal office blood pressure and elevated 24 hour ABPM). A recent workshop report from the 2005 European Society of Hypertension meeting reviewed WCH in detail [57]. The PIUMA Study [58] concluded that DBP seldom played an important part in WCH, so that daytime SBP on ABPM should be the main determinant of WCH. WCH hypertension does not appear to have the same increased risk for cardiovascular disease as sustained [59–61]. However these studies are all of relatively short duration, which may not allow enough time for transient elevations of blood pressure to be found to be associated with elevated risk. A collaborative international study of WCH showed that WCH, in a multivariate analysis of 4,406 subjects with a mean follow-up of 5.4 years, had a relative risk of stroke of 1.15 which was not significantly different from the normotensive group [62]. However, the stroke incidence rose with time such that by the ninth year of follow-up, the hazard curve for WCH crossed that of the ambulatory hypertensive group. Finally Parati and Mancia have proposed that there are at least four forms of white-coat effect, including (1) "alerting reaction": physiologic response to threatening stimulus leading to an increase in heart rate and BP, (2) "white-coat effect": alerting reaction and pressor response to measurement of BP in the clinical environment, (3) "white-coat effect, surrogate": difference between office blood pressure by physician and a measurement of blood pressure outside the doctor's office such as ABPM or home BP measurement with none of the BP measurements above normal for the environment where they were measured, and (4) "white-coat hypertension/isolated-office hypertension": office BP ≥140/90 mm Hg and normal daytime ABPM or home BP readings [63]. All of this serves to emphasis the important role that ABPM plays in the accurate diagnosis of hypertension in adults.

Children

The frequency of occurrence of white-coat hypertension in children was first reported by Hornsby as occurring in 44% (13/34) of adolescents [64]. Other authors have reported rates from as low as 12.9% [65] to as high as 88% [66]. The variance in rates is due to differences in populations sampled and to the definition used for WCH. Sorof demonstrated this as described previously with the impact of BP load on the definition of hypertension and WCH [54]. Sorof extended this work in a later review of WCH in a study of 71 children with three elevated office BP measurements and 24-h ABPM. Comparing the criteria from the Task Force paper [1] with the normal daytime ABPM values from Soergel's work [41], they found that the diagnosis of WCH was 31 vs. 59% (P<0.001), respectively [67]. More importantly, they found a strong correlation between the severity of the office blood pressure and WCH. They developed the "BP index", which was the patient's average of three office blood pressure readings divided by the Task Force's [1] 95% reading for that patient (e.g. BP index of 1.1 was a blood pressure 10% above the Task Force 95%). WCH hypertension was found in 87% of those children with BP index of 1.1, 52% with BP index of 1.1–1.2 and only 15% with BP index ≥1.2. Sorof et al. suggested that 24-h ABPM be used only in those children with BP index 1.0–1.1, or perhaps to 1.2, in order to limit the cost of ABPM. Their study did not examine the impact of nighttime ABPM and dipping status on the diagnosis of WCH.

Support for the validity of the BP index comes from Backer who found similar predictive power in the severity of blood pressure elevation in adults in the emergency room setting. For patients of all types in the ER, JNC VI stage 1 SBP elevations were associated with a 64% chance of having an abnormal follow-up clinic SBP, while for stage 3, 97% had an abnormal follow-up clinic SBP [68]. Matsuoka et al. looked at WCH in 206 normotensive and 70 hypertensive Japanese children and adolescents 6–25 years of age. A total of 33/70 (47%) children with office hypertension had WCH [69]. They observed the "white-coat effect" (office BP−daytime ABPM≥10) as described by Parati [63] in 50% of hypertensive and 25% of normotensive children. White-coat effect was strongly correlated with age, occurring in 19% (20/103) of normotensive children 6–15 years of age and 42% (14/33) of normotensive children 16–25 years of age [69]. Less is known about the adverse effects of WCH in children. Stabouli and colleagues [65] studied 85 children and found WCH in 12.9% and masked hypertension in 9.4% of these children. WCH had higher left ventricle (LV) mass index than normotensive children (27.8±5.1 vs. 25.3±5.6 g/m^2),

but this difference did not reach statistical significance. Carotid intimal thickness was also not significantly different between WCH and normotensive children. Long-term data on WCH in children are lacking.

Masked hypertension

Adults

The presence of "masked hypertension" (MH), defined as a normal casual office blood pressure and an elevated 24-h ABPM or home blood pressure has only recently been appreciated, such that it is not even discussed in the 2001 Consensus Conference on ABPM [52]. First reported by Pickering [70] as "masked hypertension" and Mancia [71] as "reverse white-coat hypertension," MH has been found to occur with a frequency similar to that of WCH. In Ben-Dov's study of 1,494 subjects using ABPM, 11% of those studied had WCH and 11% were also found to have masked hypertension [72]. MH, in contrast to WCH, has been found to have a prognosis similar to sustained hypertension. Ohkubo et al. reported on a 10-year follow up of the Ohasama study, a study of 1,332 Japanese. Analysis of cardiovascular risk (stroke and CV mortality) showed that the relative risk for masked hypertension was 2.13, very similar to that of sustained hypertension at 2.26 [73]. Although MH and WCH have been defined using ABPM, there is information suggesting that MH may be diagnosed using home blood pressure measurements. Stergiou has shown that in a study of 438 treated and untreated adults, the disagreement in diagnosis of MH by ABPM and home BP measurement was 23% for systolic and 30% for diastolic blood pressure [74]. When a 5 mm Hg "gray zone" for uncertain diagnosis was used, the disagreement fell to 9 and 6%, respectively. Bobrie and colleagues found in a study of 4,939 treated hypertensive patients (mean age 70 years), comparing office and home BP, that the hazard ratio for cardiovascular events in MH was not different from that for patients with hypertension using both office and daytime ABPM (1.96 vs. 2.06) [75].

Children

The frequency of masked hypertension in children and adolescents is very similar to what has been reported in adults. Matsuoka looked at MH in a population of 136 subjects normotensive by office blood pressure measurements with mean age 13.1±4.7 years. MH was defined as daytime SBP or DBP above the 95th percentile for sex and age or ≥135/85 for those over 15 years of age. Eleven percent of subjects were found to have masked hypertension. It was more common in boys than in girls (19 vs. 5%, $P=0.0243$), but did not differ by age (11% for patients 6–15 years vs. 12% in patients older than 15) [76]. Lurbe and colleagues reported on a study of 592 youths age 6–18 years: 34 (7.6%) had MH, 535 (34%) were normotensive and only 1% had WCH by ABPM, with 200 available for follow-up ABPM. MH was associated with a higher ambulatory pulse rate and obesity and was 2.7 times more likely to occur in those with a family history of hypertension. In a median follow-up of 37 months, 18 of the MH cases became normotensive, 13 had persistent MH and 3 had sustained hypertension on subsequent ABPM. Lurbe found that, similarly to MH in adults, MH in children is associated with cardiovascular damage when compared to normotensive children. They found that compared to normotensive controls those with persistent masked hypertension or those who developed sustained hypertension had higher LV mass index (34.9 vs. 29.6 g/m^2, $P=0.023$) and higher LV mass index above the 95th percentile (30 vs. 0%, $P=0.014$) [77]. Stergiou has preliminarily reported an ongoing study in Greece, the Araskion Study [78]. This study looks at school mercury auscultatory blood pressure measurements versus home readings with the Omron 705IT using telemetry to reduce observer bias. Unpublished results suggest a rate of WCH of 2.0% and of masked hypertension of 3.8%. However, preliminary work also questioned whether home BP recordings are truly comparable to daytime ABPM in children and adolescents for the diagnosis of masked hypertension and white-coat hypertension.

Reproducibility

Adults

A critical component of ABPM use in practice is how reproducible the results are. Mansoor looked at this issue in a study of 25 untreated hypertensive patients who had repeat office and ABPM measurements at least 3 months (median: 15 months; range: 3–80) apart. There was little difference for SBP or DBP between the first and second ABPM studies in this population [79]. Wendelin-Saarenhovi and colleagues looked at long-term reproducibility in 26 (25% hypertensive) people 65–76 years of age in whom two ABPM readings were done 4–12 months (median 8 months) apart [80]. Only mean 24-h SBP (mean difference: −3.2±7.0 mm Hg, $P<0.05$) and nighttime SBP (mean difference: −4.2±8.4 mm Hg, $P<0.05$) were significantly different between the first and second studies.

In addition to mean blood pressure values throughout the day, the patterns of blood pressure, in particular dipping status, are reproducible over time. Stefano looked at the SAMPLE study where ABPM was done at baseline, after 4 weeks placebo washout, and then after 3 and 12 months of therapy for hypertension. One hundred and seventy patients had entry and washout ABPM and two-thirds had the same dipping pattern in both studies [81]. Cuspidi reported a study of 414 younger (mean age 46±12 years), untreated hypertensive patients with two ABPM studies within 4 weeks and found that dipping status was more variable than reported by Stefano. Overall, 311 (75%) subjects had no change in dipping pattern. In normal nocturnal-dipping subjects (n=278), 219 (79%) stayed the same [82]. Of extreme dippers (n=37), only 43% remained

extreme dippers during the second study. Of subjects without dipping in the first study, only 67.6% were the same in the second study. Subjects with reproducible non-dipping patterns were older (48±12 years) than those with reproducible profile (44±12 years). In a similar fashion, Covic et al. did a prospective study on reproducibility of ABPM in patients with disease [polycystic kidney disease (PCKD) and chronic renal failure]. In these 30 patients, three APBM were done: baseline (after 3 months of normotension by office BP), 6 months and 12 months. Eleven of 30 (37%) subjects maintained the same dipping pattern during the entire period of observation [83]. From the third to sixth month, 13/30 (43%) stayed the same, 20% changing to the higher and 37% to the lower quartile. Similar outcomes were seen when comparing sixth to twelfth month and first to twelfth month.

Children

Lurbe et al. looked at the reproducibility of ABPM using the Spacelabs 90207 in 30 normotensive (<95th percentile for office BP) children with two ABPM studies done at school, a mean of 7 months apart [38]. Reproducibility for mean SBP was higher than for DBP with *R* values of 0.76 for 24-h, 0.68 for daytime and 0.79 for nighttime BP. For DBP *R* values were 0.68 for 24-h, 0.68 for daytime and 0.51 for nighttime DBP.

Bald looked at single blood pressure comparisons in 28 children. In random order their BP were taken with the auscultatory mercury standard, Spacelabs 90207 and a DINAMAP (GE Healthcare Technologies, Waukesha, WI) [23]. Compared to the mercury standard, the Spacelabs overestimated SBP by 5 mm Hg (range: 2–10 mm Hg) while the DINAMAP underestimated DBP by 8.5 mm Hg (range: 1–13 mm Hg). When ABPM was done in these 28 children, tolerability was good in younger children (<12 years with 78% completing the measurements). It was significantly better in the children above 12 years with 91% completing the ABPM ($P<0.001$) although there were both day and night failed individual readings in both groups. In 1999, Lurbe did a similar study in 333 patients, 11.1±3.7 years of age [84]. A total of 281/333 (84%) had more than 80% valid readings over 24 h; 213/333 (64%) had more than 90% of expected readings. The two factors in multivariate analysis that correlated with successful readings were age and higher SBP.

Rucki and colleagues looked at repetitive ABPM in 59 children 8–19 years of age with elevated office blood pressure and ABPM 1 year apart using the Spacelabs 90207. On the first ABPM, 28 were hypertensive. On second ABPM, only 54% were still classified as having hypertension. The mean decrease in daytime SBP was 4.5 mm Hg and in DBP 2.7 mm Hg. Nocturnal mean SBP fell 2.3 mm Hg, and DBP was not significantly different [85]. Of the 31 who were initially normotensive by ABPM, at 1 year 23% were classified as hypertensive with the only significant difference a 3.5 mm Hg rise in nighttime SBP.

Using the same study design, O'Sullivan looked at 50 teenagers in Newcastle with the TM 2421. He looked at the tracking of casual BP, 24-h school, 24-h home, 24 night and total 24-h ABPM. The strongest correlation (*R*) values at 1 year follow up were for total 24-h SBP at 0.79, all other measures having *R* values of 0.61 or less [86]. Using tertiles of initial 24-h ABPM, 24-h SBP had the strongest tracking while casual DBP had better reproducibility than any of the 24-h values of ABPM DBP.

Stergiou looked at casual, home and ABPM reproducibility in 16 subjects (8 hypertensive, 3 high normal and 5 normotensive by Task Force office criteria), 8–17 years of age. Casual blood pressure was the least reproducible, with home blood pressure readings having similar but not quite as good reproducibility compared to all measures of 24-h ABPM [87]. As an example, *R* values were 0.63 for casual SBP, home SBP 0.74, 24-h 0.87, awake 0.76 and asleep 0.79. Diurnal patterns, similarly to those in adults, had much lower reproducibility with *R* values for awake–asleep differences of 0.62 for SBP and 0.14 for DBP.

Flynn and colleagues suggested that ABPM in children may be used to distinguish between primary and secondary forms of hypertension. Eighty-five children (40 with primary and 57 with secondary hypertension) underwent ABPM. Mean age of the population was 13.8±3.5 years and those with secondary hypertension were younger and leaner than the primary hypertension subjects. In this population there were strong correlations for daytime DBP load of ≥25% (20.8% primary vs. 65%, secondary, $P<0.005$) or a nocturnal SBP load of ≥50% (37.5% primary vs. 75% secondary, $P=0.02$) and for both of these together (8.3 vs. 40%, $P=0.03$) [88]. Secondary hypertension had lesser drops in nocturnal SBP (9±5 vs. 12±5, $P=0.006$) and DBP (15±10 vs. 18±7), but these differences were not seen when only untreated patients were analyzed.

Reproducibility of ABPM may also differ by ethnicity. Barnes looked at 41 African American children with high office BP and three determinations of ABPM. There was no difference in mean 24-h, daytime, and nighttime for SBP or DBP, nor any significant difference in mean MAP [89]. Harshfield looked at 186 youths [94 African Americans (37 males) and 92 European Americans (40 males)] with mean age at initial ABPM of 14± years and at second ABPM of 16± years. The two ethnic groups had similar daytime SBP by ABPM but higher nighttime SBP at both initial and follow-up ABPM (109±9 vs. 105±8 and 110±10 vs. 105±8, both $P<0.001$) [90]. This was associated with higher LV mass and height as well. Of the variance between the first and second ABPM in African Americans, male gender accounted for 17% and age for 10%, while for night SBP male gender accounted for 18% and age 12%. In European Americans, height accounted for 11% of variance in daytime SBP with no contribution of gender and for nighttime SBP, gender accounted for 13% and height 8% of variance between the first and second ABPM.

Chase looked at the differences in office and ABPM in Anglo ($n=50$), Hispanic ($n=32$) and African American

(n=36) adolescents and young adults. The office mean SBP and DBP were not different between the two groups [91]. Mean night SBP and DBP were higher for males than females in all three ethnic groups. The values for day ABPM values trended towards African Americans being higher than Anglo and Anglo higher than Hispanic subjects but these differences did not reach statistical significance, likely due to sample size (124±8 vs. 121±6 vs. 117±7, respectively). Harshfield looked at the issue of body size and its impact on the differences in ABPM reported between African Americans and Caucasians. In a multiple regression model they found a race-by-height interaction for nighttime SBP in African Americans but not Caucasians. There was a race-by-weight interaction for nighttime SBP and DBP in African Americans but only for nighttime DBP in Caucasians with a weaker interaction for nighttime SBP for Caucasians. A race-by-body surface area was seen for nighttime DBP in African Americans only [92].

Reproducibility also involves monitoring performance and physician interpretation. Amoore assessed 14 Spacelabs 90207 and one 90217 for measurement consistency over a period of 6 years using a blood pressure simulator. All 15 monitors at all pressures measured less than a 2 mm Hg difference 89.5% of the time, with a maximum difference of 4.5 mm Hg [93]. Considerable variation existed in interpretation of ABPM results in children by subspecialists. In reviewing ABPM in 92 children, three nephrologists agreed only 64% of the time on the diagnosis of the hypertension [94]. The disagreement was based predominantly on the value of blood pressure load used by each nephrologist to diagnose hypertension by ABPM in children.

Additional uses of ABPM

The use of ambulatory blood pressure monitoring is increasing in adult medicine due to the multiple insights into the hypertensive patient it offers that are not obtainable with office blood pressure measurement. In adults, ABPM has a much higher correlation with cardiovascular outcomes than does office blood pressure measurement [95–97]. Nocturnal blood pressure recordings ("dipping status") provide information that is not available from office or home blood pressure measurements. Dipping status has been reported to be an independent predictor of mortality and morbidity, including cardiovascular death, stroke, cerebrovascular disease and dementia [98–103]. Recently, interest has focused on the rise in blood pressure with awakening or "morning surge" as a predictor of cardiovascular disease [104–106]. ABPM has been found to be altered by disease states such as sleep apnea [107], autonomic dysfunction [108], and renal disease [109], and to reveal different impacts of antihypertensive therapy compared to office blood pressure readings [110]. Hadtstein from Soergel and Wuhl's group defined normative values for circadian and ultradian rhythms in a study of 938 healthy children. In this study, 90% of children displayed circadian BP rhythm independent of age [111]. Puberty had a marked effect on ultradian rhythms (6-h and 12-h monitoring).

There is increasing information about ABPM in special populations of children, especially those with renal disease. ABPM had stronger correlations than office blood pressure with glomerular filtration rate and the presence of hypertension in children with chronic renal failure [112]. ABPM was better at diagnosing hypertension than office BP and had a strong association with renal length, volume and the number of renal cysts in children with cystic renal disease [113, 114]. The extent of scarring from chronic pyelonephritis or vesicoureteral reflux was strongly correlated with ABPM in a study of 61 children [115] but did not correlate better than casual office blood pressure in children with isolated microhematuria [116]. In chronic, stable children after renal transplantation, ABPM was better at detecting high rates of hypertension than casual office blood pressure, [117, 118] but did not correlate well with the left ventricular mass index in these children, suggesting that the cardiac hypertrophy seen may have a mechanism beyond hypertension [118]. In children after hemolytic uremic syndrome, daytime ABPM was not different in those children with and without renal insufficiency. Nocturnal dipping however was significantly blunted in patients with HUS and renal insufficiency and not in those with normal renal function after HUS [119].

In children and young adults 7–21 years of age with hypertrophic cardiomyopathy (HCM), symptomatic patients showed a significantly lower systolic blood pressure in the morning and a higher dissociation of heart rate variability and blood pressure response than normal controls [120]. This study suggested that ABPM may be predictive for cardiac events in young patients with HCM. In children with Riley-Day syndrome (familial dysautonomia), ABPM was able to identify the severe vasomotor instability with hypotension and hypertension during the day, with a preserved circadian rhythm in a study of three subjects [121]. Several authors have shown that, in children and adolescents after surgical repair of aortic coarctation, daytime hypertension was seen in roughly a third of these patients [122, 123]. ABPM also found nocturnal hypertension in patients with daytime normotension in the larger of these studies [123]. Sleep-disordered breathing in children also has strong correlations with ABPM. Thirty-nine children with obstructive sleep apnea (OSA) were compared to 21 with primary snoring. Children with OSA had significantly greater mean blood pressure variability during wakefulness, a higher night-to-day systolic BP and smaller nocturnal dipping of mean BP [124]. ABPM has been performed successfully in infants and toddlers using the Spacelabs 90207 device. In a study of 97 children 2–30 months of age, a satisfactory ABPM profile was obtained in 86.6% of the children with an average of 75% satisfactory readings. SBP and DBP increased with length (height) and nocturnal decreases in SBP and DBP were small [125]. Normal values for this population have yet to be determined.

Use of ABPM in children and adolescents in clinical practice

Despite the volume of information about the diagnosis and treatment of hypertension provided by ABPM [126, 127], there is still considerable disagreement about its use in adults [128, 129]. These issues focus primarily on the cost of ABPM, despite a recent analysis showing that in a chronic disease state such as hypertension, ABPM can lower the long-term cost of hypertension despite the ABPM high per-test cost [130]. In children, the Task Force 2 has not reached consensus guidelines on use of ABPM. In a small study, Flynn demonstrated that ABPM could have a beneficial impact on the management of hypertension in children [131]. But the issue remains how best to integrate ABPM into the care of children with hypertension, particularly increasing the awareness of masked hypertension in children, a less appreciated and more dangerous issue than white-coat hypertension.

White's discussion of the use of ABPM [129] offers an excellent model, advocating use of home blood pressure measurement to focus the use of ABPM on those patients that would most benefit from ABPM. Home blood pressure measurement has been found to correlate well with daytime ambulatory blood pressure in adults [132, 133] and in children [87, 134] although others have found [78], particularly in children with renal disease [135], that home self-measured BP may be lower than daytime ABPM values. Home blood pressure measurement has also been found to improve hypertension control in adults [136]. Similar data on improvement of BP control with home monitoring are lacking in children. Despite the questions raised above, home blood pressure measurement is frequently recommended by clinicians, and the blood pressure obtained at home used to make clinical decisions in hypertension in children [137].

Conclusions

When to use ABPM

ABPM is an important tool in the management of hypertension in children, which due to its expense needs to be applied judiciously. ABPM could be justified in at least the following four circumstances. First, Sorof [67] has shown that the BP index (ratio of child's BP to the 95th percentile by Task Force 1) can predict which children would benefit from ABPM. The maximum benefit for use of ABPM is in those children with BP index of 1.0–1.2, i.e. those within 20% of the 95th percentile target. Children with BP index above 1.2 are highly likely to have true hypertension and not WCH. Secondly, ABPM is appropriate when home blood pressure readings are in disagreement with office readings, i.e. in cases of suspected WCH or masked hypertension. Third, if the child has target organ damage (proteinuria, left ventricular hypertrophy, etc.) from hypertension despite normal office readings, ABPM should be considered. Fourth, the presence of resistant hypertension is indicative for ABPM use, although a consultation with a pediatric hypertension specialist before the ABPM measurement might be most appropriate.

What normal values should be used for ABPM in children

I have previously expressed my preference for the work of Wuhl and the "LMS" method of determining normal values for ABPM in children [138]. This should be the lead reference for ABPM normal values until such time as a formal Consensus Conference occurs. In addition to normal values, assessment of the blood pressure load should also be a part of the diagnosis of hypertension in children when using ABPM. Here again until a Consensus Conference occurs, values for blood pressure load of greater than 25% [54] or 30% [55, 56] should be considered abnormal.

Finally home blood pressure measurement should be offered in all children where it is socially and psychologically appropriate to aide in diagnosis of both masked hypertension and white-coat hypertension. ABPM should still be used to confirm the diagnosis in children where these conditions are suspected due to the current concern about the absolute accuracy of home blood pressure determinations in children. Combining these three observations should allow cost-effective utilization of ABPM in children and enhance the care of hypertension in children.

Future research

There are still many unanswered questions about ABPM and home blood pressure monitoring in children. Devices for both need validation studies in children and perhaps alterations in the oscillometric algorithms to know that the measurements with these devices are accurate. The Task Force must look at the normative data for ABPM and formally endorse values for ABPM. A standard definition of blood pressure load should also be determined to improve consistency of diagnosis of hypertension in children using this parameter. Finally, further information about whether other blood pressure measurement techniques such as repeated nonambulatory blood pressure measurement [139] or shorter periods of ambulatory blood pressure determinations [140] would aide in the diagnosis of hypertension in children as they have in adults should be explored.

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