Pediatric ambulatory blood pressure monitoring: diagnosis of hypertension

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Abstract Pediatric hypertension (HTN) is a growing concern and should be diagnosed and treated aggressively to reduce the global disease burden. Ambulatory blood pressure monitoring (ABPM) is a useful clinical tool providing a more accurate description of the patient's blood pressure (BP) than office BP measurements, and can be considered the “gold standard” in the evaluation of the pediatric patient with a concern for HTN. The American Heart Association have suggested criteria for diagnosing ambulatory HTN, and research continues into further clarification of how to best utilize the large volume of data obtained from an ABPM report. ABPM has some limitations; however, the advantages far outweigh these. Routine use of ABPM is recommended among clinicians to better evaluate and assess the severity of a child's HTN, and for proper management in order to prevent target organ damage and the resulting sequelae, thereby reducing the burden of cardiovascular risk in hypertensive children and adolescents.

Keywords ABPM · Pediatric hypertension · Ambulatory blood pressure monitoring

The epidemic of obesity along with hypertension (HTN) and cardiovascular disease is a major growing contributor to global disease burden [1, 2]. The prevalence of HTN and pre-HTN in children and adolescents has continued to increase over the last decade, to nearly 4 % and 10 % respectively [3]. Pediatric HTN remains one of the strongest predictors of adult HTN [4], which significantly increases the cardiovascular mortality risk in adults [5, 6]. The prevalence of adult HTN and the resulting sequelae will continue

to increase further unless there is more aggressive screening, diagnosis, and treatment of HTN in children.

Although it is critically important to identify young hypertensive patients who need intervention, HTN and pre-HTN are frequently undiagnosed in pediatric populations [7]. Measuring blood pressure (BP) is difficult in children. BP levels vary on a minute-to-minute basis in response to a variety of physiological and environmental stimuli, which also makes BP measurement challenging. Ambulatory BP monitoring (ABPM) may overcome these challenges and help to properly characterize BP level and variability for better risk stratification and prediction of cardiovascular disease outcomes. ABPM uses a portable automated BP device that provides multiple BP measurements during regular activities throughout the day in the home (and school) environment and is the only method that allows BP measurement during sleep; therefore, ABPM is felt to provide a more accurate description of the patient's BP than office BP measurements, also eliminating the possibilities of improper technique and observer bias. Use of ABPM with established norms has allowed confirmation of true HTN even in children as young as 5 years old. White-coat HTN (WCH) is extremely common in children with incidence exceeding 40 % [8, 9]. ABPM is especially useful, and the only available method, to identify WCH in children who are anxious in the medical setting, as well as those with masked HTN with normal BP in the clinic, but elevated BP by ABPM. The prevalence of masked HTN is ~9 % in the general pediatric population [10] and can be as high as 38 % in children with chronic kidney disease [11]. ABPM also makes the diagnosis and treatment of nocturnal HTN possible, providing important information about the health of the cardiovascular system during sleep. ABPM HTN is associated with left ventricular hypertrophy (LVH) [12, 13] and progression to end-stage renal disease in children who have chronic kidney disease [14]. The use of ABPM to manage HTN has been shown to prevent progression of carotid intima-medial thickness in renal transplant recipients

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[15]. In addition, ABPM has been shown to be cost-effective in the evaluation of pediatric HTN [16]. Twenty-four-hour ABPM is now well established as a useful clinical tool in the evaluation of the pediatric patient who has elevated BP or is at risk of elevated BP, and application of ABPM will help clinicians improve BP control and reduce the burden of cardiovascular risk in hypertensive children and adolescents.

One important limitation of ABPM, however, is the lack of set guidelines for the diagnosis of HTN utilizing the large volume of data obtained from a single complete 24-h ABPM recording. An ABPM report often contains over 50 discrete BP readings taken at 20- to 30-min intervals while awake during the day and 30- to 60-min intervals at while asleep at night. At least one valid reading per hour, including during sleep, is necessary for a study to be considered complete [17]. Invalid readings are eliminated by the device software, and readings are then used to generate several key assessments, including average systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP) during the day-time (awake BP) and night-time (sleep BP), and over the entire 24 h. The readings are compared with established norms to determine associated BP load, defined as the percentage of valid ambulatory BP measures above the set 95th percentile of BP for age, gender, and height [18], which is also provided in the report for both day and night, and over the entire 24 h. ABPM also provides information on nocturnal dipping, the normal reduction in BP that occurs with sleep, for both SBP and DBP. Recent research, in both adults and children, has begun to clarify the best approach to the application of an ABPM data set for interpretation of the HTN status of patients with elevated office BP. Diagnosis of ambulatory HTN and determination of the severity of BP elevation is made using both the office BP reading obtained by auscultation and the results of the ABPM study.

It is important to recognize that ABPM measurements made in the middle of a normal and active day with an oscillometric device tend to be higher than BP obtained with auscultation in seated children after 5 min of rest; hence, established ambulatory BP norms should be used as opposed to Task Force BP data [19]. The normative German ABPM data in the collaborative study by Soergel et al. [20] and the smoothed values by Wühl et al. [21] currently provide the reference values for interpretation of ambulatory BP in children. Separate tables for normative data are available for boys and girls by both age and height. It is preferred to use the tables for height, since height is an important determinant of BP in children, except in children less than 120 cm tall, in whom it may be necessary to use the tables by age, which do go down to 5 years [22]. The American Heart Association (AHA) updated these values and, in 2008, after some modifications of the work by Lurbe and colleagues [23], proposed the criteria for the classification of children as either normotensive or hypertensive by ABPM,

as outlined in Table 1 [17]. Although the classification scheme in the AHA statement provides important information for the clinician to diagnose HTN, it does not provide guidance on how to analyze all the data obtained in an ABPM recording. Some questions still remain about the diagnosis of HTN by ABPM.

Blood pressure load and mean

Mean ABPM values can be assessed for the entire 24-h period or for the awake and asleep periods separately. Mean BP levels generated by the ABPM are compared with normative values to determine whether a subject's BP is normal or elevated. Mean BP alone does not provide information regarding BP variability, manifesting as large amplitude fluctuations above and below the 95th percentile value. BP load provides additional information on the true HTN burden in a specific patient. It has been suggested that both mean BP and BP load should be used to define ambulatory HTN. However, some patients with normal mean BP levels may have elevated BP loads. In adults, the BP load is more predictive of hypertensive end-organ injury than is mean BP [24], and normotension defined solely as mean 24-h BP less than the 95th percentile may be insensitive to the risk of hypertensive end-organ damage. BP loads in excess of 25 % are typically considered elevated [24] and loads in excess of 50 % have been demonstrated to be predictive of LVH [12]. Children with normal mean BP and elevated loads can be at risk of target-organ damage and may need antihypertensive therapy, even if they do not fit into the proposed criteria for the diagnosis of ambulatory HTN.

Systolic and diastolic blood pressure

Typical BP measurements include an SBP and a DBP value, representing the extremes of pressure fluctuation within the circulation during the cardiac cycle. There has been much debate about whether SBP or DBP HTN is more predictive of adverse cardiovascular outcomes. In routine clinical use of ABPM, it is apparent that some children have isolated DBP HTN. Based on AHA criteria, children with DBP HTN may be overlooked. It is likely that it is not a benign condition; isolated DBP HTN may be associated with a lower cardiovascular risk, but there is a high probability of transition to systolic–diastolic HTN [25, 26]. DBP HTN on ABPM in children has been shown to potentially indicate the presence of underlying secondary causes of HTN [27], and has been shown to be associated with increased incidence of LVH in children on dialysis [28]. DBP load and mean are also important in diagnosing HTN in children, at least to filter out those who will require closer follow-up and

Table 1 The American Heart Association (AHA)-suggested schema for the staging of ambulatory blood pressure (BP) levels in children (adapted from Urbina et al. [17], used with permission)

Classification	Clinic BP ^a	Mean ambulatory SBP ^b	SBP load, %
Normal BP	< 95th percentile	< 95th percentile	<25
White coat HTN	> 95th percentile	< 95th percentile	<25
Masked HTN	< 95th percentile	> 95th percentile	>25
Pre-HTN	> 95th percentile	< 95th percentile	25–50
Ambulatory HTN	> 95th percentile	> 95th percentile	25–50
Severe ambulatory HTN (at risk of end-organ damage)	> 95th percentile	> 95th percentile	>50

HTN hypertension, SBP systolic blood pressure

^a Based on the National High Blood Pressure Education Program Task Force Standards

^b Based on the ABPM values of Soergel et al. or the smoothed values of Wühl

not necessarily antihypertensive therapy. There is, however, a striking lack of variability of diastolic ambulatory BP in the normative data [29] and measurement of DBP by the oscillometric technique with ABPM is not as accurate as mercury measurements made using the auscultatory method. This makes the diagnosis of DBP HTN difficult.

Mean arterial pressure

Mean arterial pressure (MAP), the time-weighted average of BP during the entire cardiac cycle, is an excellent way to evaluate stress on the walls of the vessels and to assess perfusion pressure seen by target organs. MAP provides another indication of overall circulatory pressure load and has also been proposed to have prognostic relevance in assessing cardiovascular outcomes [14, 30, 31]. Treatment guided by ambulatory MAP was shown to reduce the rate of progression of CKD in the recently published ESCAPE trial, further highlighting the importance of this ambulatory BP parameter [14].

In the study by Suláková and Feber published in this issue of *Pediatric Nephrology* [32], the authors showed that the addition of MAP in the definition of ABPM hypertension in children would increase the detection of hypertension by 19 %. Suláková and Feber also point out that it may be more appropriate to utilize MAP to classify the results of ABPM studies, since this is the one BP parameter that is measured directly by the majority of devices used to perform ABPM in children, using the oscillometric technique, which directly measures MAP and back-calculates SBP and DBP using manufacturer-specific software algorithms. The calculated SBP and DBP values have been shown to vary significantly compared with SBP and DBP values obtained by auscultation. The inclusion of MAP into the ABPM definition may allow for earlier detection of BP abnormalities in children and prediction of cardiovascular outcome.

Nocturnal blood pressure and dipping

Currently, no guidance exists on how to evaluate isolated nocturnal HTN and declines in BP during sleep (dipping) on ABPM, both of which have significant prognostic implications. Nondipping describes a pattern of a blunted sleep-related fall in mean SBP or DBP (<10 %). Among adults, “nondippers” have been reported to be at greater risk of increased left ventricular mass index (LVMI) and morbid cardiovascular events [33]. Isolated nocturnal HTN and nondipping is reported to be highly prevalent in children with chronic renal insufficiency, on dialysis and after transplantation [28, 34]. Greater nocturnal SBP load on ABPM has been found to be highly specific for a secondary cause of HTN in children [27]. In addition, nocturnal HTN predicts the severity of obstructive sleep apnea [35] and the development of microalbuminuria in diabetic adolescents [36]. Lesser degrees of nocturnal dipping can be associated with LVH in children on dialysis [28]. Isolated abnormalities of sleep BP on ABPM should be taken into consideration when reading an ABPM report. Although there are not enough data on the importance of nocturnal HTN in lower-risk pediatric populations, the definition of a normal ABPM study probably should include normal nocturnal BP and normal dipping.

Blood pressure variability

Detecting BP variability (BPV), estimated by the standard deviation or coefficient of variance for daytime or night-time readings on ABPM, is straightforward, but not readily done in pediatric practice. Twenty-four-hour BPV is found to be increased in obese children [37] and has been reported to correlate with glomerular filtration rate and albuminuria in young patients with chronic renal insufficiency [38]. Patients with increased BPV have overall greater organ damage and LVMI at follow-up compared with those hypertensive patients in whom BPV is less, but who have the same 24-h BP mean

values [39]. BPV has been shown to be predictive of stroke and other cardiovascular events in adults, and specific antihypertensive agents have been found to be superior to other drugs in reducing BPV and adverse vascular events [39–41]. Larger prospective pediatric studies are required in which BPV can be assessed as an additional independent factor contributing to cardiovascular risk in HTN, and to determine whether drugs and combinations of drugs that reduce both mean BP and BPV will have a beneficial effect on cardiovascular outcome. Abnormal diurnal variability should be considered important information in assessing HTN in a young patient's ABPM. The duration of action and time of administration of antihypertensive medications are likely to be important considerations in reducing BPV, although lack of sufficient data in children makes this recommendation more difficult to implement.

Accurate assessment of HTN in children is the cornerstone of the better prevention of its deleterious effects. ABPM has become an essential clinical and research tool in day-to-day practice. Despite numerous studies in the literature, there are still gaps in our knowledge of how best to utilize ABPM data. Suláková and Feber [32] have made an important contribution to this rapidly developing field, but much more research is needed to clarify the best approach to the use of the ABPM data set in children. Information on the usefulness of circadian BP control, BP surge (the difference between morning BP and the nadir during sleep) as well as correlations between BP variability and target-organ damage in hypertensive children, is required for the fine-tuning of antihypertensive management. Clinical management recommendations based on outcome studies performed in pediatric patients are surely needed for clinicians who, having diagnosed WCH and masked HTN by ABPM must decide if these results require drug therapy for the prevention of target-organ damage. Currently available normative data [20] are based on mostly Caucasian children with small numbers of shorter children in the database, making the analysis of ABPM studies difficult in children with impaired growth, specifically in children with chronic diseases. Better normative data across different ethnic backgrounds are needed in order to understand the true prevalence of HTN in our communities. However, the advantages of ABPM far outweigh these limitations, and, hence, ABPM has been shown to be a powerful tool for assessing BP in pediatric patients and is now considered by many pediatric nephrologists to be the gold standard for measuring BP in children. The routine use of ABPM among clinicians managing pediatric HTN is sure to grow, hopefully guided by careful trials performed in children.

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