Published in final edited form as:

Prog Pediatr Cardiol. 2016 June ; 41: 67–73. doi:10.1016/j.ppedcard.2015.12.001.

Hypertension in chronic kidney disease: role of ambulatory blood pressure monitoring

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Abstract

Children with chronic kidney disease have a markedly increased risk of cardiovascular morbidity and children with end stage renal disease have an estimated 30 times greater risk of cardiovascular mortality than the general pediatric population. In adults, the link between hypertension and cardiovascular disease is well-documented but that association has not been so readily apparent in children with chronic kidney disease. This may be in part because the early changes in blood pressure that occur in these patients do not necessarily manifest with changes in casual blood pressure measurements. Ambulatory blood pressure monitoring, with its ability to gather multiple readings both during the normal activities of the day and the night, is felt to be a more veritable measure of blood pressure. Its use in children has been hampered by limited data on normative values and difficulties in blood pressure classification, while its use in adults is ever expanding. However, with an increasing number of studies in children with chronic kidney disease, ambulatory blood pressure has revealed a greater prevalence of abnormal findings in this population and has been shown to better predict cardiovascular risk than current standards. Two large multi-center studies in Europe and North America have revealed even greater utility of ambulatory blood pressure measures in this population. It is hoped that continued use of ambulatory monitoring in children will help overcome some of its perceived limitations while also validating its use in those at high risk of cardiovascular morbidity.

Keywords

Ambulatory blood pressure monitoring; Chronic kidney disease; Diurnal variation; Hypertension; Left ventricular hypertrophy; Masked hypertension

1. Introduction

Ambulatory blood pressure monitoring has been in use for nearly four decades in the adult population [1], however its application has become more commonplace in clinical and

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research use in that population over the last 15 years. Like other medical technologies, ambulatory blood pressure monitoring use in the pediatric population has lagged behind that of their adult counterparts with reasons for its limited use having varied from technical restrictions of the devices and a dearth of expertise to a lack of standardized measures and subjective definitions of hypertension. However, as this technology is being studied to a greater degree in pediatrics, its utility in certain populations is being fully recognized. One of the populations of great interest is children with chronic kidney disease, as they not only have a greater risk of cardiovascular morbidity but they also have a higher incidence of abnormal ambulatory blood pressure findings. Children with chronic kidney disease have increased rates of left ventricular hypertrophy [2-4], abnormal flow mediated vasodilation [5], and carotid intimal medial thickening [6] while the mortality rates of children who progress to needing maintenance dialysis are 30 times greater than the general pediatric population with cardiovascular disease being the leading cause [7]. Rates of abnormal ambulatory monitoring findings, mainly masked hypertension, is around 7% in the general pediatric population [8], but are several-fold higher in children with chronic kidney disease. Thus, this population may be ideally suited to be the “torchbearer” for studies using ambulatory monitoring and the development of standards of care and utilization. This review addresses the advantages and limitations of ambulatory blood pressure monitoring use in children with chronic kidney disease, provides data gathered to date from its use in that population, and discusses its potential for future use.

2. Advantages and Limitations of ABPM in Pediatric CKD

Blood pressure has traditionally been performed as a single measurement obtained in the physician’s office under certain idealized conditions (at rest for five minutes with arm held level to the heart). Though these measurements may be performed repeatedly, with at least three elevated readings recommended to make the diagnosis of hypertension [9], this casual blood pressure reading, a single snapshot in the course of the entire day, has been the “gold standard” determinant of hypertension [10]. This is mainly based off its practicality to perform, as it is a simple process that can easily be taught and replicated, so it has utility as a screening measure for the general population. Technological advancements, such as oscillometric techniques and micro-chip technology, led to the advent of ambulatory blood pressure monitoring, allowing for multiple accurate automated blood pressure readings throughout a continuous period and now using a variety of cuff sizes. Proponents of ambulatory blood pressure monitoring argue that this method gives a “truer” measure of blood pressure [11]. Firstly, it assesses blood pressure during normal daily activities, not the artificial scenario which takes place in the physician’s office. Therefore, much like a Holter monitor or a stress test compares to an in-office electrocardiogram, ambulatory blood pressure monitoring reflects blood pressure during the normal vicissitudes of daily activities rather than a single instant. Secondly, ambulatory monitoring provides multiple measures over time, and therefore may be more reliable and reproducible, while also being less susceptible to observer bias. Lastly, the diurnal measures over 24 hours of monitoring may account for circadian rhythms and other contributors to blood pressure variability that cannot be captured by other standard measurement methods [12].

Because 24 hour ambulatory monitoring gives multiple blood pressure readings over time, monitoring results may be analyzed in different ways, each with its own strengths and weaknesses. Blood pressure may be analyzed as an averaged measure, like 24- hour mean, daytime mean, or nighttime mean blood pressure. Averaged values are not robust parameters, are possibly skewed by extreme values, and do not yield information on frequency of blood pressure elevation. However they offer much more consistent information than a single measurement. Ambulatory monitoring also allows for assessment of blood pressure load, or the frequency in which readings exceed a certain parameter, typically the 95th percentile. Although blood pressure load does reflect how *often* blood pressure is excessive, it cannot tell you how *much* it is excessive. Therefore, interpretation of both mean values and overall blood pressure load may help in determining overall risk [13].

Normative data in children

For a long period of time, ambulatory blood pressure studies in children were limited by a lack of normative data for this population. In 1997, the largest cross-sectional cohort of nearly 1150 children receiving ambulatory blood pressure monitoring [14] reported their findings as a basis for normative data. Five years later, a separate, slightly smaller study of almost 950 children was able to report data such that standardized scores were able to be derived [15]. The data from these two studies comprise the current normative data standards for pediatric ambulatory blood pressure monitoring, with cut point values slightly higher than those reported for casual blood pressure readings by the Fourth Report on High Blood Pressure in Children and Adolescents [9]. The discrepancies between the ambulatory and casual blood pressure standards may be explained by differences in measurement method, as ambulatory standards are based off oscillometric measurements, which are known to be higher, while casual standards are derived from auscultative measures. Others attribute the slight elevation in ambulatory measures to the expected rise in blood pressure during normal daily activities. The ambulatory normative data has other limitations, not just in total numbers of patients, but also in the age and heterogeneity of patients, as both study populations were comprised mainly of taller, healthy German schoolchildren. Additionally, the data reported from these studies showed very little variability in diastolic blood pressure values across age groups and heights, unlike the auscultative norms in children, calling into question the validity of these measures.

Ambulatory blood pressure classification

Using these ambulatory blood pressure standards and comparing to casual measures, an overall classification system was established, first in adults [16], but also in children [17]. Familiar classifications include normotension, when the casual and ambulatory results (mean AND load) are both normal, and white coat hypertension, when the casual blood pressure is elevated but ambulatory results (mean AND load) are normal. Ambulatory hypertension, which may be thought of as confirmed hypertension, is when both the casual and ambulatory measures are elevated. Masked hypertension, once termed reverse white coat hypertension, is when there is a normal casual blood pressure reading but elevated ambulatory (mean OR load) findings. The currently recommended schema of classification for children was updated in 2014 [18] and is summarized in Table 1.

The addition of blood pressure load parameters along with mean ambulatory measures expanded the number of abnormal ambulatory monitoring results and, thus, capturing more individuals at potential risk. However, it also added more strata in the classification system. Having more than half of all ambulatory blood pressure readings above the 95th percentile, i.e. a blood pressure load >50%, is classified as severe ambulatory hypertension and is appropriately considered higher risk for end organ injury. Also, an elevated blood pressure load with normal ambulatory means (load NOT mean) but slightly elevated casual blood pressure measures would be classified as pre-hypertension. The most recent updates to this classification system [18] had modification of casual blood pressure cut-offs for normotension and pre-hypertension being changed from the 95th to 90th percentile. However, despite the addition of further strata, there are still ambulatory monitoring results that may not fit into any of the current categories. Also, the currently recommended classifications do not account for other factors (systolic vs. diastolic, day vs. night) which may have greater prognostic significance.

Diurnal variation

Through the observation of patterns over a full 24 hours, it was discovered that blood pressure has diurnal variation, with decreased measures during sleep. [19] This physiologic “dipping” is normally a 10% decrease from the mean daytime blood pressure while sleeping. Lack of this relative decrease, or “non-dipping”, can only be detected by 24 hour ambulatory monitoring. In Figure 1, two different abnormal ambulatory blood pressure patterns are displayed. Isolated daytime hypertension (Figure 1B) differs from diurnal hypertension (Figure 1A) by the presence of appropriate dipping shown in the middle third of all of the ambulatory values. This finding would otherwise be undetected if not for 24 hour monitoring and may be of greater significance, especially in those individuals with normal daytime measures.

Non-dipping has been attributed to different etiologies, including volume expansion and increased sympathetic stimulation [20, 21], and has been thought to indicate secondary causes of hypertension, including chronic kidney disease [22]. However, the presence of non-dipping has also been seen with higher prevalence in African American adults and children [23, 24]. Non-dipping may have an independent role in determining cardiac end organ injury in hypertensive adult patients [25], while it has been associated with more rapid progression of renal injury in adults with diabetes and IgA Nephropathy [26, 27].

Abnormal ambulatory results and association with end organ injury

Although it is unclear as to which of the features of ambulatory monitoring- the multitude of readings, reproducibility, diurnal results-provides its greatest advantage, ambulatory blood pressure monitoring has been found to be superior to casual blood pressure results in predicting cardiovascular morbidity [28]. Adult studies in the general population have shown better correlation with ambulatory than casual blood pressure readings in left ventricular mass [29] and carotid intimal medial thickness [30]. Many pediatric studies have similarly been able to confirm the stronger relationship between ambulatory blood pressure findings and left ventricular mass including the development of left ventricular hypertrophy [31], while the association with vascular changes, such as carotid artery stiffness and decreased

distensibility, has only been seen in pediatric renal transplant patients to date [32]. As prevention of target organ injury is the ultimate goal, ambulatory monitoring looks to be a powerful predictive tool and may be used more selectively in populations at higher susceptibility to cardiovascular morbidity, like chronic kidney disease. To this end, the American Heart Association (AHA) Atherosclerosis, Hypertension, and Obesity in Youth Committee has recently amended its recommendations for the use of ambulatory blood pressure monitoring in children with certain conditions to add chronic kidney disease, along with obesity and obstructive sleep apnea, to a list which previously included diabetes mellitus, solid organ transplant (kidney, liver, heart), and coarctation of the aorta [18]. Table 2 gives the complete list of conditions.

3. Studies to Date of Ambulatory Monitoring Use in Pediatric Chronic Kidney Disease

As renal disease in children is both less prevalent and has less readily evident or symptomatic cardiovascular morbidity than in adults, some of the first ambulatory blood pressure studies in this population focused on subsets of pediatric chronic kidney disease with perhaps the highest cardiovascular risk, children with end stage renal disease. Like most initial investigations, these reports were simply observational in nature. Lingens et al. first reported prevalence of hypertension by ambulatory measures in 35 pediatric dialysis subjects, analyzing both peritoneal and hemodialysis patients [33]. They noted that 70% of the patients on peritoneal dialysis were hypertensive on ambulatory measures, in contrast to only 35% of the hemodialysis patients. Comparing ambulatory and casual blood pressure measures, they found that one-third of the patients with normotension on pre-dialysis blood pressure measurements would be re-classified as having hypertension based on ambulatory measures, in essence having masked hypertension. Similarly, one-third of patients that were hypertensive by casual readings were classified as normotensive by ambulatory results. Two years later, a similar study by the same group looked at 27 pediatric renal transplant recipients, comparing their ambulatory and clinic blood pressure measures [34]. They too found that 37% of subjects would have their blood pressure status re-classified using ambulatory, compared to casual, standards. Additionally, 30% of subjects were found to have attenuated dipping at night and were considered at added risk, which we now know to be true. These initial observations were mirroring the results being seen in adult studies of these same populations [35] with high rates of ambulatory monitoring abnormalities, such as masked hypertension and nocturnal non-dipping, seen. Masked hypertension has been reported to be prevalent in 7-11% of the general pediatric population [36] and these higher prevalence rates in children with chronic kidney disease were replicated in later studies of these high risk pediatric populations [37-38].

The association of masked hypertension with left ventricular changes was first described in the general adult population by Liu et al. in 1999 [39] and confirmed in the Italian population PAMELA study in 2001 [40]. Similar associations of left ventricular hypertrophy with increased mean 24-hour and nighttime systolic BP [41] and decreased “dipping” [42] were seen in hypertensive children without renal disease. However, there had been no data linking hypertension to the left ventricular changes seen in high prevalence in children with

chronic kidney disease. Therefore, it seemed plausible to take the next step and investigate whether the changes on ambulatory blood pressure monitoring could be connected with the development of end organ injury seen in pediatric chronic kidney disease, as there is a higher prevalence of masked hypertension in this population.

A cross sectional study of 29 children with mild to severe (Stage 2-4) chronic kidney disease by Mitsneces et al. sought any correlation between casual blood pressure, ambulatory blood pressure measures, and echocardiogram findings. [43] They found that 24-hour mean systolic blood pressure directly correlated with left ventricular mass index, while no relationship with casual blood pressure was seen. These authors also followed these subjects longitudinally over two years and noted that the left ventricular mass index increased significantly over that time. One-third of subjects with normal left ventricular mass index at the study's onset had developed left ventricular hypertrophy [4]. Increased night-time systolic blood pressure was independently associated with increased left ventricular mass over time. These single center studies, however, were limited in their total number of subjects, as many pediatric chronic kidney disease studies tended to be, so were not able to clearly establish the link between hypertension and left ventricular hypertrophy that had been done in adults with chronic kidney disease.

The first large multi-center study of children with chronic kidney disease utilizing ambulatory monitoring was a randomized control clinical trial conducted in Europe called the ESCAPE trial [44]. This landmark study recruited 385 children with mild to severe (Stages 2-4) chronic kidney disease across 33 centers throughout the continent. Children were included in the study if their 24-hour mean arterial pressure on ambulatory monitoring was either elevated or controlled only with the use of antihypertensives. Subjects were then randomized to receive the angiotensin converting enzyme (ACE) inhibitor ramipril to try and achieve either strict, <50th percentile, or conventional, <90th percentile, blood pressure control again using 24- hour mean arterial pressure readings. The primary purpose of this study was to see if kidney disease progression could be significantly slowed with stricter blood pressure control, which it was. However, as ambulatory monitoring was performed every 6 months over the course of 5 years in this large cohort, there was a surfeit of available ambulatory blood pressure data.

Unfortunately, the study authors did not find an association between the development of left ventricular hypertrophy and ambulatory blood pressure results. Some have attributed this lack of finding of association to the use of a fixed, and not age-adjusted, cutoff for left ventricular hypertrophy that was used in the trial. This may, in part, explain the higher incidence of left ventricular hypertrophy, 33%, which was seen in trial participants. Despite this lack of findings linking ambulatory blood pressure abnormalities and end-organ injury, this was the first large trial in pediatric chronic kidney disease utilizing ambulatory blood pressure parameters to steer treatment decisions and it yielded additional information about the utility of ambulatory monitoring for future pediatric studies.

The other large multi-center study examining ambulatory blood pressure parameters in children with chronic kidney disease is the Chronic Kidney Disease in Children (CKiD) study [45]. This prospective cohort study has recruited nearly 600 children with mild to

moderate (Stages 2-3) chronic kidney disease from 48 centers in North America starting in 2006. One of the four main aims of the study is to examine the impact of chronic kidney disease on cardiovascular risk factors, with in depth analysis of casual and ambulatory blood pressure measures along with echocardiogram results at regularly prescribed intervals. Unlike the ESCAPE trial, this cohort study is purely observational with interventions, including the use of anti-hypertensive medications, being completely at the discretion of local providers. A cross-sectional analysis of initial ambulatory blood pressure findings revealed 18% of subjects having confirmed (ambulatory) hypertension and 38% having masked hypertension [46]. Additionally, 15% of those with confirmed and 29% of those with masked hypertension were not prescribed anti-hypertensives, revealing how often hypertension is being undertreated in this at-risk population. Left ventricular hypertrophy was found in 17% of subjects, with a higher prevalence seen in those with African American descent, shorter duration of chronic kidney disease, nephrotic range proteinuria, and lacking ACE inhibitor or angiotensin receptor blocker (ARB) use. In this cohort, left ventricular hypertrophy was four times more likely to be present in subjects with masked hypertension than those with normotension, offering the first link between blood pressure findings and left ventricular hypertrophy.

Further analysis of the ambulatory monitoring results for this cohort was later reported by Samuels et al. [13] Subjects receiving any anti-hypertensive medication had a 13% higher odds of having normal ambulatory monitoring results than those not on any medication, which was not statistically significant. However, those subjects receiving an ACE inhibitor were 89% more likely to have normal ambulatory results, which was significant. A faster decline in renal function or an increase in proteinuria over time was also associated with having an abnormal study. Lastly, with the large number of ambulatory studies performed, 13% of studies were not easily classified by the original schema proposed by the AHA [17], applicable at that time. These subjects, most of which have ambulatory pre-hypertension on the newer classification schema, were classified as having masked hypertension, as they were considered at higher risk for cardiovascular changes. In hindsight, this re-classification was likely justified as masked hypertension was associated with left ventricular hypertrophy even with the inclusion of these subjects with 'less severe' ambulatory abnormalities, but it also allows for potential skepticism as to the strength of this association.

Other smaller studies published in the same time period or subsequent to the ESCAPE trial and CKiD study have reiterated many of the same findings of these larger studies, with one exception. In 2008, Dionne et al. reported their findings in 42 children with chronic kidney disease Stages 2-4 [47]. Abnormalities of ambulatory measures were noted in 49% of their subjects who otherwise had normal clinic blood pressure findings. They also noted that the percent of nocturnal dipping decreased as kidney function decreased. Sinha et al. reported a high percentage of masked hypertension, 43%, and left ventricular hypertrophy, 62%, in their study of 49 children with chronic kidney disease [48]. Although 24 hour mean systolic, diastolic, and arterial pressures were all significantly different between subjects with and without left ventricular hypertrophy, they reported that clinic systolic blood pressure was the most important factor in determining risk of left ventricular hypertrophy. This contrasts with nearly all the previous studies which found no correlation between casual blood pressure and end organ injury. Most recently, Gupta et al. reported their ambulatory blood pressure

findings in 46 children with moderate to end stage renal disease (Stages 3-5) [49]. Despite a lower prevalence of masked hypertension of only 20%, they noted that the higher the numbers of abnormal ambulatory indices, namely 24-hour mean blood pressure, blood pressure load, and nocturnal non-dipping, the greater likelihood of having LV hypertrophy.

4. Future Considerations

An updated statement from the AHA Youth Committee recently called for an “urgent need for more comprehensive normative ambulatory blood pressure data” across gender, race, and age [18]. There have been studies which have looked at the applicability of ambulatory blood pressure in infants and toddlers [50- 51], verifying that it technically can be performed in this younger population while also gathering data for these age groups as a basis to establish some normative standards. Standards for younger age groups may not be as essential for progress in the pediatric chronic kidney disease population, as hypertension may be less prevalent in younger patients. Non-glomerular etiologies of renal disease, like obstructive uropathy and renal dysplasia, are vastly more prevalent in younger patients, with much less likelihood of salt and fluid retention. Glomerular causes of chronic kidney disease have a higher prevalence of hypertension seen in children [52]. Perhaps a much greater need in the pediatric chronic kidney disease population of the United States is the validation of normal ambulatory standards in non-European children. African-American children are already at an increased risk of having unrecognized hypertension and developing cardiovascular morbidity in chronic kidney disease [52], but there are other racial and ethnic groups who also need validated norms as well. Similarly, as one set of ambulatory blood pressure standards is based off a minimal height of 120 cm, and children with chronic kidney disease often have some degree of growth impairment, establishing normative data for shorter patients may also be a more practical need for this population.

Better data establishing the links between ambulatory blood pressure findings and cardiovascular morbidity in higher risk pediatric patients, like chronic kidney disease, is absolutely essential. Data-driven skeptics often cite the lack of data with ambulatory blood pressure monitoring use as justification against recommending its use in children. In fact, the most recent published recommendations on blood pressure management in children with chronic kidney disease came from the international Kidney Disease Improving Global Outcomes (KDIGO) workgroup in 2012. They clearly states that “there is insufficient trial evidence to recommend the use of ambulatory blood pressure monitoring in this guideline”. [53] This echoes similar recommendations from the Kidney Disease Outcomes Quality Initiative (KDOQI) from almost a decade earlier [54]. However, the European Society of Hypertension’s pediatric workgroup acknowledges this as a flawed approach. They dissent that a complete lack of any data, which is where things stood with children only one decade ago, does not invalidate any extrapolations of data from adult studies to children with chronic kidney disease who have a risk of cardiovascular morbidity closer to that of adults [21].

More studies in this select population, as has been taking place, are needed to simultaneously validate the use of ambulatory monitoring to the guideline analytics while also establishing what ambulatory abnormalities- non-dipping, blood pressure load, mean

systolic or diastolic-provide the greatest risk in these patients. One study in children without secondary hypertension has shown that night-time systolic blood pressure load and daytime systolic variability have been associated with increased left ventricular mass [55], while another study found mean daytime systolic blood pressure to be a better predictor in children with metabolic syndrome [56]. Similar studies in the pediatric chronic kidney disease population may then help in establishing the most critical ambulatory blood pressure findings based off greatest cardiovascular risk, in this specific population.

Once ambulatory blood pressure monitoring is validated as a more accurate measure of cardiovascular risk, then the next logical step is its utilization in assessment of efficacy of anti-hypertensive therapy in interventional studies, especially in children. Just as individuals can have masked hypertension, individuals taking anti-hypertensive medications can have masked uncontrolled hypertension or MUCH. Rates of masked uncontrolled hypertension have been reported to be up to 31% of general adult patients that were previously deemed to have controlled blood pressure [57]. A very recent study in adults with chronic kidney disease reported prevalence rates up to 56%, almost doubled the rate of the general adult hypertension population, when utilizing night-time ambulatory monitoring data in combination with daytime blood findings [58]. Employing ambulatory monitoring results to guide anti-hypertensive dosing and timing has been recommended in resistant hypertension in adults [59]. Additionally, Hermida et al. noted that adult chronic kidney disease patients who administered only one of their anti-hypertensive medications at night time had significantly lower mean night-time blood pressure readings and one-third the risk of cardiovascular events [60]. Therefore, 24-hour ambulatory monitoring may better assess the efficacy of chronotherapy, or the timing of therapeutics. This adjusting of anti-hypertensive medications based off ambulatory blood pressure results is not a novel concept in children. It has already been done in children with chronic kidney disease, as the ESCAPE trial used ambulatory results to adjust ramipril dosing as part of their protocol. Data from the ambulatory studies performed as part of this trial showed that there was 39% less variability in ambulatory measures compared to casual blood pressure readings [61]. Using a power analysis with this reduced variability, the researchers reasoned that using ABPM in drug efficacy studies could reduce sample size needs from 55-75%. Because of the general paucity of pediatric patients with hypertension and subsequent difficulty in recruitment for interventional studies, use of ambulatory monitoring would seem very prudent.

5. Conclusions

Ambulatory blood pressure monitoring has made advances in its use in pediatrics over the past decade, especially among populations at higher risk of cardiovascular morbidity like with children with chronic kidney disease. Progress in this area of investigation was first slowed by a lack of normative data and verified classification system in pediatrics. However, studies in children with chronic kidney disease have made a steady progression first validating a high prevalence of ambulatory blood pressure abnormalities in children with chronic kidney disease and then comparing ambulatory and casual blood pressure findings in their prediction of end organ injury in this population. This trajectory has mirrored that of adult chronic kidney disease patients; however it has been more plodding with limited numbers of patients and less readily evident cardiovascular morbidity to evaluate within

single academic centers. Despite these obstacles, a majority of pediatric chronic kidney disease studies have verified the superiority of ambulatory measures over causal blood pressure findings, consistent with adult data, and the most recent large cohort study has linked ambulatory blood pressure abnormalities with the development of left ventricular changes.

Despite the claims of analytic pundits that there is insufficient evidence to recommend ambulatory monitoring use, it seems that well-designed pediatric studies of sufficient subject numbers consistently conclude its benefit over currently used standards of predicting cardiovascular risk. It appears that the past projections made by pediatric hypertension and nephrology experts that ambulatory monitoring be considered the “gold standard” for blood pressure evaluation in children with chronic kidney disease have been verified. Moving forward, it is hoped that the lessons learned from the ESCAPE trial and the future learnings from the CKiD study will help us overcome any of the perceived shortcomings of ambulatory monitoring in children so that it may be utilized in higher risk populations, much like is being done currently in adults.

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Figure 1.
Different Ambulatory Blood Pressure Monitoring Patterns: A) Both Daytime and Night-time Hypertension; B) Isolated Daytime Hypertension

Table 1**Suggested Revised Schema for Staging of Ambulatory BP Levels in Children**

Classification	Office BP*	Mean Ambulatory SBP or DBP ^{†‡}	SBP or DBP Load, % [§]
Normal BP	<90th %tile	<95th %tile	<25
White coat hypertension	95th %tile	<95th %tile	<25
Prehypertension	90th %tile or >120/80 mm Hg	<95th %tile	25
Masked hypertension	<95th %tile	>95th %tile	25
Ambulatory hypertension ^{//}	>95th %tile	>95th %tile	25–50
Severe ambulatory hypertension (at risk for end-organ damage)	>95th %tile	>95th %tile	>50

%tile indicates percentile; BP, blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

* Based on National High Blood Pressure Education Program Task Force normative data.^{1c1a}

[†] Based on normative pediatric ABPM values in Appendix Tables A1 through A4.

[‡] For either the wake or sleep period of the study, or both

[§] For patients with elevated load but normal mean ambulatory BP and office BP that is either normal (<90th percentile) or hypertensive (≥95th percentile), no specific ambulatory BP classification can be assigned based on current evidence and expert consensus. These “unclassified” patients should be evaluated on a case-by-case basis, taking into account the presence of secondary hypertension or multiple cardiovascular risk factors.

^{//} Some clinicians may prefer the term *sustained hypertension* rather than *ambulatory hypertension*.

Table 2

Conditions in which Ambulatory Blood Pressure Monitoring (ABPM) may be particularly helpful

Condition	Relevance of ABPM
Secondary hypertension	Elevated load, abnormal dipping and variability
Chronic kidney disease	Prevalence of hypertension, masked hypertension, association with target-organ changes and disease progression
Types 1 and 2 diabetes mellitus	Abnormal circadian variation, association with microalbuminuria and vascular changes
Obesity	Masked hypertension, correlation between BMI and hypertension severity, abnormal dipping, association with target-organ damage
Sleep apnea	Hypertension severity, abnormal circadian variation
Genetic syndromes Neurofibromatosis type 1 Turner syndrome Williams syndrome	Abnormal BP patterns indicating secondary cause of hypertension, especially renal artery stenosis and aortic coarctation
Treated patients with hypertension	Response to antihypertensive medications and/or lifestyle changes
Hypertension research	Reduction in subject number in drug trials

ABPM indicates ambulatory blood pressure monitoring; BMI, body mass index; and BP, blood pressure.