



REVIEW ARTICLE

Importance of ambulatory blood pressure monitoring in the diagnosis and prognosis of pediatric hypertension

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Target organ damage

Abstract The prevalence of high blood pressure (BP) at pediatric age has increased progressively, one of the causes of which is obesity. However, the dominant etiology in this age group is renal and/or cardiovascular pathology. Ambulatory blood pressure monitoring (ABPM) is the method of choice for the diagnosis of hypertension, especially in children at high cardiovascular risk. Its use is limited to children from five years of age. Choosing appropriate cuff size is key to obtaining correct blood pressure.

The main indication for ABPM is to confirm the diagnosis of hypertension. It also allows the diagnosis of white coat hypertension (which may represent an intermediate stage between the normotensive phase and hypertension), or masked hypertension, associated with progression to sustained hypertension and left ventricular hypertrophy (LVH). Children with isolated nocturnal hypertension should be considered as having masked hypertension.

BP load is defined as the percentage of valid measurements above the 95th percentile for age, gender, and height. Values above 25-30% are pathological and those above 50% are predictive of LVH. ABPM correlates with target organ damage, particularly LVH and renal damage. It is useful in the differentiation of secondary hypertension, since these children show higher BP load and less nocturnal dipping, and confirmation of response to therapy. Thus ABPM allows the diagnosis and classification of hypertension, provides cardiovascular prognostic information and identifies patients with intermediate phenotypes of hypertension.

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Importância da monitorização ambulatória da pressão arterial no diagnóstico e prognóstico da hipertensão arterial em idade pediátrica

Resumo Em idade pediátrica a prevalência da hipertensão arterial (HTA) tem aumentado progressivamente, sendo a obesidade uma das responsáveis. Apesar disso, a etiologia dominante nesta faixa etária é a patologia renal e/ou a cardiovascular. A monitorização ambulatória de pressão arterial (MAPA) é o método de eleição para o diagnóstico de HTA, especialmente em crianças com risco cardiovascular elevado. O seu uso está limitado a crianças a partir dos cinco anos. A seleção do tamanho da braçadeira é o ponto chave na obtenção de leituras corretas da tensão arterial (TA).

O MAPA tem como principal indicação a confirmação do diagnóstico de HTA. Também permite diagnosticar hipertensão da bata branca (que pode representar um estádio intermédio entre a fase normotensa e a hipertensão), ou hipertensão mascarada, associada a progressão para hipertensão mantida e HVE. As crianças com HTA noturna isolada devem ser consideradas como portadoras de hipertensão mascarada. A carga tensional é definida como a percentagem de medições válidas acima do p95 para a idade, sexo e estatura, sendo que valores superiores a 25-30% são patológicos e superiores a 50% são preditivos de hipertrofia ventricular esquerda (HVE). O MAPA correlaciona-se com lesão de órgão alvo, nomeadamente com a HVE e a lesão renal. É útil na diferenciação da hipertensão secundária, já que estas crianças manifestam maiores cargas tensionais e menor dipping nocturno, e na confirmação da resposta à terapêutica.

Assim, o MAPA permite o diagnóstico e a classificação da HTA, fornece informação prognóstica cardiovascular e identifica doentes com fenótipos intermédios de HTA.

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Introduction

One in four adults worldwide is hypertensive. The prevalence of hypertension at pediatric age is increasing,¹⁻⁴ particularly in developed countries,⁵ with recent data showing prevalences around 4% and that of prehypertension reaching 10%.² In Portugal, a study by Maldonado et al.⁶ analyzing 5381 children found that 12.8% were hypertensive.⁶

Increasing obesity has led to changes in blood pressure (BP) patterns, including elevated BP levels in children and adolescents.^{1,5} Sustained adiposity and hence higher BP in childhood will tend to increase the prevalence of hypertension and its complications in adulthood.^{3,7-9} Obesity is the cardiovascular risk factor with the strongest relationship with BP, and higher body mass index is associated with progression from prehypertension to hypertension.¹⁰ However, the dominant etiology of hypertension in this age-group is renal and/or cardiovascular pathology.⁷

Definition of hypertension

The definition of hypertension in children has undergone significant changes in recent decades.⁸ The European Society of Hypertension (ESH) guidelines, published in 2016,⁴ classified resting BP values for children aged 0-15 years (Table 1) based on percentiles, while for those aged 16 or older the consensus was that the definitions used should be based on the absolute cut-offs used for adults.

Hypertension in children is generally defined as systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) at or above the 95th percentile on three or more separate occasions.^{2-4,11}

The ESH guidelines⁴ also stress the importance of isolated systolic hypertension (ISH), the clinical significance of which in youth is still debated. ISH is the most prevalent form of elevated BP in adults aged over 50 years and its causes are multifactorial.

Neonatal hypertension has been defined as SBP at or above the 95th percentile for gender, gestational age and postnatal age. Its incidence is low (0.2-3%) and a history of umbilical catheterization is an important risk factor.¹² The importance of intrauterine and early life events in the development of cardiometabolic disease in adult life has been underlined.⁴ The time immediately before and after birth is a sensitive period in which multiple interactions between hemodynamic and metabolic parameters may contribute to risk of cardiometabolic disease.⁴ Target organ damage (TOD) has been reported in persistent neonatal hypertension.¹³

Birth weight affects ambulatory BP, with various studies showing an inverse relationship with daytime SBP.^{1,2} Premature infants born with intrauterine growth restriction have higher nocturnal BP in childhood and adolescence.^{2,10} BP monitoring is advisable from an early age in such high-risk cases,¹³ while regular BP measurement is recommended for all children from the age of three years.

Methods of blood pressure measurement in children

Office measurement, home readings or ambulatory monitoring?

Office BP measurement is the first step in identifying children with suspected hypertension.² However, BP values are

Table 1 Classification of hypertension in children and adolescents.

	0-15 years	16 years and older
Normal	<p90	<130/85 mmHg
High-normal	≥p90 to <p95	130-139/85-89 mmHg
Hypertension	≥p95	≥140/90 mmHg
Stage 1 hypertension	p95 to p99 plus 5 mmHg	140-159/90-99 mmHg
Stage 2 hypertension	>p99 plus 5 mmHg	160-179/100-109 mmHg
ISH	SBP ≥p95 and DBP <p90	≥140/<90 mmHg

p90: 90th percentile; p95: 95th percentile; p99: 99th percentile; DBP: diastolic blood pressure; ISH: isolated systolic hypertension; SBP: systolic blood pressure.

subject to dynamic variations due to interactions among neurohormonal, behavioral and environmental factors.⁹ BP is around 10% higher during waking hours than during sleep. An office BP measurement thus merely reflects a single point of a circadian variable.^{7,14} BP measurement under normal day-to-day conditions gives a more reliable figure than one obtained in the artificial environment of the physician's office.¹⁵

Home ('self-measured') BP assessment is widely used in adults. However, it has two serious limitations in children: the lack of home devices that have been validated in the pediatric age-group, and the lack of accepted normative data for home BP levels in children.²

Ambulatory blood pressure monitoring (ABPM) is well established for the assessment and treatment of hypertension in adults (including the elderly and pregnant women¹⁷) but has only relatively recently been used in children,^{2,16} the first reports dating to the 1990s.¹⁸ It is now the method of choice for diagnosis and therapeutic monitoring in pediatric age-groups,^{3,8,9,14,17,18} especially in children at high cardiovascular risk.¹⁹ The first consensus document on application and interpretation of ABPM in children and adolescents was published in 2008¹ and updated in 2014.¹⁰

Although home BP measurement is more reliable and consistent than office measurements,^{3,14} its diagnostic sensitivity is only 81% and it is thus not recommended as an alternative to ABPM.^{1,9,20}

Methodology of ambulatory blood pressure monitoring in children

Equipment

Many of the recommendations for ABPM in adults are also applicable in children, but there are substantial differences.

The equipment should be light and sturdy, and able to tolerate some subject movement without giving excessive error readings.^{1,17} Pediatric patients and their parents need to understand how the apparatus functions and be aware of the importance of keeping the arm still during BP readings.¹

Selection of the cuff is key to obtaining accurate BP readings. The width of the cuff should be 40%, and its length should be 80% of the mid-arm circumference,^{1,3,17} measured at a point midway between the acromion and the olecranon. The cuff should be applied to the non-dominant arm to avoid interference with school work, unless contraindicated (for example due to an arteriovenous fistula).^{1,10} If there is a

significant BP discrepancy between the arms, the monitor should be placed on the arm with the higher BP.

There are two techniques for measuring BP: oscillometric and auscultatory.¹ Despite the known limitations of oscillometry, this is the technique used in most centers, as well as in the development of reference tables.^{1,3,17} Its main advantages are ease of use and fewer erroneous readings.

Age

Although some trials have successfully included younger children, routine use of ABPM is limited to those aged five years or more.¹

The proportion of successful measurements increases from 87.5% at younger ages to 92.7% in older children, due to the fact that older children and adolescents are more likely to cooperate in performing the measurement correctly.¹⁸

Frequency of assessment

The software controlling the ABPM monitor can be programmed to record every 15-20 min throughout the 24 hours, adjustable from every 15 to 20 min during waking hours and from every 20 to 30 min during sleep.¹⁰ The most common protocol is every 20 min during the day and every 30 min at night.¹

The best way to identify periods of wakefulness and sleep is by the patient recording times of waking and sleeping in a diary.⁸

Most authors consider that a minimum of one or two readings per hour are required to consider an ABPM study to be interpretable.^{1,9,10} A sufficient number of valid BP recordings would be at least 40 to 50 readings for a full 24-hour report and 65-75% of all possible BP readings for a partial day report (depending on the protocol used).¹ Periods of over two hours without a valid reading compromise the quality of the exam.¹⁰

Physical activity

An important concern in interpreting ABPM data in pediatric patients is how to divide the recording into sleep and wake times. This is usually done through the times of sleeping and waking recorded in the patient diary.¹

When accounting for levels of physical activity, most hypertension specialists recommend that children undergoing ABPM should continue their normal activities but refrain from contact sports and vigorous exercise.¹ ABPM is also incompatible with water sports.⁷ Children should be told to

Table 2 Interpretation of ambulatory blood pressure monitoring results and classification of hypertension.

	Office BP	Ambulatory MAP	BP load (%)
Normal	$\leq p90$	$< p95$	<25
WCH	$\geq p95$	$< p95$	<25
Prehypertension	$\geq p90$ or $> 120/80$ mmHg	$< p95$	≥ 25
MH	$< p95$	$> p95$	≥ 25
Stage 1 hypertension	$> p95$ to $< p99$ plus 5 mmHg	$< p95$	25-50
Stage 2 hypertension	$\geq p99$ plus 5 mmHg	$\geq p95$	25-50
Stage 3 hypertension	$\geq p99$ plus 5 mmHg	$\geq p95$	>50

p90: 90th percentile; p95: 95th percentile; p99: 99th percentile; BP: blood pressure; MAP: mean arterial pressure; MH: masked hypertension; WCH: white coat hypertension.

stop moving and talking when the cuff inflates and to keep the arm still with the cuff at heart level.²¹

Diary

Children and their parents should be instructed to maintain a diary in which they record sleeping and waking times, naps, activities that may influence BP measurements, including stressful situations or exercise, and timing of anti-hypertensive medications.^{1,10}

Symptoms such as dizziness should also be recorded, because up to 91% of children with a history of syncope demonstrate postural hypotension on ABPM.¹⁰

Interpretation of ambulatory blood pressure monitoring

Values that fall outside of the following range should be discarded^{10,17}:

- SBP 60-220 mmHg
- DBP 35-120 mmHg
- Heart rate 40-180 bpm
- Pulse pressure 40-120 mmHg.

Mean arterial pressure

Most ABPM devices calculate the 24-hour value of mean arterial pressure (MAP), the mean of SBP and DBP, and, on the basis of diary entries for sleeping and waking times, daytime and nocturnal MAP.^{1,10} These values can then be compared with reference values in order to interpret the exam.¹ It is preferred to use the tables for height, except in children less than 120 cm tall, in whom it may be necessary to use the tables by age.⁹

Reference values are provided by the German Working Group on Pediatric Hypertension, published in 2002. However, this data set has several limitations: it includes only central European white children and relatively few shorter children (<140 cm in height), and shows a striking lack of variability in ambulatory DBP values. Thus, many authors consider that these normative values may not be representative of the normal ambulatory DBP in all pediatric patients.¹⁰

It should be noted that BP values obtained from ABPM should not be interpreted with reference to values from single measurements,^{1,9} since ABPM values tend to be higher than the latter.^{9,10}

Blood pressure load

BP load is defined as the percentage of valid measurements above the 95th percentile for age, gender and height.^{1,8,17} Like MAP, it can be calculated for the entire 24-hour period or for daytime and nocturnal periods separately.¹

BP loads in excess of 25-30% are considered pathological^{1,2} and those in excess of 50% have been demonstrated to be predictive of left ventricular hypertrophy (LVH).^{8,17}

A combination of MAP and BP load is used to categorize ABPM results as normal or abnormal (Table 2).^{1,8,10}

Nocturnal dipping

Dipping refers to the physiological decline in BP during sleep, normally of $\geq 10\%$ in mean SBP and DBP.^{1,8,9,16,17}

ABPM is the only method that can measure nocturnal BP, which cannot be estimated by single measurements either at home or in a clinical setting.²⁴

A fall of less than 10% (non-dipper pattern) correlates with a higher likelihood of TOD and worse cardiovascular prognosis.^{7,9,16,22} This pattern is also seen in cases of sustained adrenergic stimulation, such as those resulting from disorders of the adrenal glands.

Blood pressure variability

ABPM is also useful in the assessment of BP variability, which has prognostic value. The activity of BP regulatory systems is needed to meet the changing physical and psychological demands of a normal day.¹ Increased BP variability has been demonstrated in obese children and is most likely related to increased sympathetic nervous system activation. In adults, greater BP variability has been correlated with the development of hypertensive LVH.¹

Indications for ambulatory blood pressure monitoring

The main indication for ABPM is to confirm the diagnosis of hypertension, whether true hypertension, white coat hypertension (WCH) or masked hypertension (MH).¹⁶

The recommendations for ABPM are listed in Table 3.^{3,4}

White coat hypertension

One of the most important indications for ABPM is to exclude WCH.^{1,7,9}

Table 3 Recommendations for ambulatory blood pressure monitoring.*During the process of diagnosis*

To confirm hypertension before starting antihypertensive drug treatment
TOD and normal office BP
Type 1 and 2 diabetes
Chronic kidney disease
Renal, liver or heart transplant
Severe obesity
Hypertensive response during exercise testing

During antihypertensive drug treatment

Evaluation of refractory hypertension
Assessment of BP control in children with TOD
Symptoms of hypotension

Other clinical conditions

Autonomic dysfunction
Suspicion of catecholamine-secreting tumors

BP: blood pressure; TOD: target organ damage.

WCH is defined as BP levels that are the 95th percentile or higher when measured in the physician's office or clinic but are completely normal (average BP <90th percentile) outside of a clinical setting.¹ It is a transient, stress-induced elevation of BP associated with the medical examination,² and is especially pronounced in younger patients, especially those aged under 12 years, and in obese patients.² Its incidence ranges between 22% and 40%, depending on the series,^{1,2,4,17} similar values to those seen in adults.¹⁸

The likelihood of WCH decreases as office BP increases; children with office BP >10% above the 95th percentile are more likely to be true hypertensives.¹

WCH may not be entirely benign.² In adults with normal ABPM, BP variability increases with increasing BP and is associated with TOD (cardiovascular system, kidneys, central nervous system and retina³).¹⁰

Several studies have shown that although left ventricular mass in children with WCH is within normal ranges, it is greater than in control groups, which means that these children should be closely monitored. Other forms of TOD, such as endothelial dysfunction and increased carotid intima-media thickness, are also associated with higher ABPM levels.¹ In fact, WCH may represent an intermediate stage between normotension and hypertension,¹⁰ and some studies suggest that these children should be treated as having prehypertension.¹⁶

Masked hypertension

ABPM may also identify MH, defined as a normal office BP but elevated ambulatory levels.^{1,2,21} This condition, the etiology of which is poorly understood,²⁴ in children is associated with progression to sustained hypertension and LVH,¹⁶ in a similar way to children with hypertension confirmed by ambulatory BP measurements.²⁴

MH may be suspected when there are previous reports of elevated clinical BP from other providers such as primary health care, or if the presence of LVH is inconsistent with the office BP.^{1,2,10}

An excessive BP response to exercise testing, which has been observed in children with WCH, may also be a manifestation of MH, and in such cases ABPM is recommended. Longitudinal studies have shown that SBP during exercise is positively associated with future resting SBP, independently of resting SBP and other cardiovascular risk factors.⁴

The prevalence of MH has not been clearly determined, ranging from 5.7% to 15% in different studies.^{1,3,4,9,10,16} It is more common in obese children,²² especially if they display a non-dipper pattern.¹⁰ It is also found in other conditions including diabetes, cardiomyopathy, hyperthyroidism,^{7,16} and obstructive sleep apnea.⁹

Children with isolated nocturnal hypertension should be considered to have MH and the same significance should be attributed as to daytime hypertension. Its incidence is higher in children who have been transplanted (38%) and those with chronic kidney disease; renal transplantation appears to be a major risk factor for MH.^{9,22} Other factors include a high-salt diet and a sedentary lifestyle.²²

Prehypertension

Prehypertension is defined as office BP \geq 90th percentile or $>120/80$ mmHg¹¹ and mean ambulatory BP <95th percentile with elevated BP loads.¹⁰ It is recognized as a condition that requires assessment and follow-up, due to the risk of progression to sustained hypertension.¹⁰

Patients with prehypertension demonstrate abnormalities on ABPM intermediate between normotensive and truly hypertensive people.¹⁰ ABPM can be very helpful in stratifying risk for TOD, because even with normal mean BP, increased BP variability is associated with TOD in adults.¹

Adolescents with prehypertension already have higher LVM values, lower glomerular filtration rate, and increased urine protein excretion, as well as greater carotid intima-media thickness, than normotensive control subjects.¹⁰

Assessment of risk for target organ damage

LHV, thickening and stiffening of large arteries and urinary albumin excretion are the most easily assessed markers of TOD.³ LHV remains to date the most thoroughly documented form of TOD caused by hypertension in children and adolescents.³ The prevalence of LHV in children with hypertension is 8–41%, depending on the criteria used to define both hypertension and LHV; studies that use age-specific reference intervals show higher prevalences.^{4,23}

Renal damage is rarely seen in children with essential hypertension, but these patients have higher albuminuria levels. The severity of albuminuria correlates with LHV.⁴

In adults, ABPM, particularly nocturnal SBP and BP load,¹ is a better marker of TOD,²⁰ especially with LHV, than office BP readings. It also correlates better with renal damage as indicated by albuminuria. The albumin/creatinine ratio is strongly related to variability of DBP.¹

Higher SBP values at the age of 12 years are associated with carotid intima-media thickening in adulthood, which in turn is correlated with higher risk for developing atherosclerosis at older ages.^{3,4} Changes in vascular function are also more common in children with higher BP levels.^{3,10}

Assessment of secondary hypertension

Secondary hypertension is more common in children than in adults.³ Hypertension detected in very young children, or in children with systemic conditions and a diagnosis of stage 2 hypertension, is suggestive of secondary hypertension.¹ The likelihood of identifying a secondary cause of hypertension is inversely related to the age of the child and directly related to the degree of BP elevation.³

ABPM may be useful in differentiating primary from secondary hypertension, since children with secondary hypertension manifest greater nocturnal SBP loads and greater daytime and nocturnal DBP loads, as well as decreased nocturnal dipping.^{1,16}

Assessment of efficacy of antihypertensive therapy

ABPM is useful for assessing response to antihypertensive therapy and to identify those with uncontrolled hypertension, especially in patients with isolated nocturnal hypertension¹⁶ or secondary hypertension,¹⁰ in cases of apparently drug-resistant hypertension, or when the symptoms of hypertension are suspected of being secondary to medication.^{1,14,16}

ABPM is also valuable in the identification of periods of hypertension when medication is ineffective, in order to optimize the timing of medication with respect to circadian BP patterns.¹⁶

Characterization of blood pressure profile in children with chronic disease that could lead to hypertension

Hypertension is common in children and adolescents with chronic renal disease. It has a very high prevalence in children undergoing dialysis, in whom 40% of mortality is due to cardiovascular causes.²⁰

Non-dipping in patients undergoing dialysis may be an independent predictor of poor cardiovascular outcomes.²⁰

Since the reference values were obtained in healthy children, there are doubts concerning their applicability in children with chronic conditions such as renal disease, as well as concerning determination of the ideal BP values for children at risk for hypertension.⁷

Some authors argue that in children with chronic renal disease, BP should be maintained below the 50th percentile for age and gender. Hypertension is a determining factor for progression to renal failure, and so prompt treatment is protective and can avoid the need for renal replacement therapy (dialysis or transplantation), improving survival and quality of life.⁷

Isolated nocturnal hypertension is common in children undergoing solid organ transplantation (22–41% of cases) and various studies have shown that it is the most frequent type of hypertension in these patients.²² Its etiology is multifactorial, the main causes being steroid therapy, sodium retention, chronic rejection, and stenosis of the transplanted renal artery.²²

Cardiovascular risk factors

Total adiposity and insulin resistance have been correlated with a high prevalence of the nondipping phenomenon, as has higher salt intake.¹

Abnormally elevated daytime and nocturnal BP levels, and diminished dipping, have been demonstrated in

children with type 2 diabetes. These changes may be related to subclinical vascular damage⁷ and renal disease and may be an early marker for renal deterioration.^{1,22}

In unilateral multicystic dysplastic kidney, ABPM is of particular value for the early detection of elevated BP, in view of the risk of secondary damage to the contralateral kidney.⁷

Daytime BP variability is increased and a non-dipper pattern is observed at night in 68.7% of children with obstructive sleep apnea.^{1,16,21}

Higher MAP levels are seen on ABPM in sedentary children, those subjected to psychosocial stress and those medicated with stimulants, such as in attention deficit hyperactivity disorder.¹

Contraindications

The contraindications for ABPM are^{1,17}:

- Coagulation disorders
- Cardiac rhythm disorders (e.g. atrial fibrillation)
- Known allergies to elements of the monitoring device.

Although serious adverse events such as venous thrombosis have not been reported in children, mild sleep disturbances,¹ petechiae and ecchymosis¹⁷ have been documented.

Conclusions

The prevalence of hypertension in children and adolescents is rising worldwide, largely due to increased adiposity. Timely diagnosis of hypertension in children can potentially reduce the risk of future cardiovascular disease.⁵

ABPM enables the diagnosis and classification of hypertension, provides cardiovascular prognostic information²⁰ and identifies patients with WCH or MH, which are intermediate phenotypes of hypertension.²⁴

Conflicts of interest

The authors have no conflicts of interest to declare.

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