Section A-Research paper

Diagnostic Evaluation of Hypertension among Children

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Abstract

As with any medical condition, appropriate diagnostic evaluation is a critical component in the evaluation of a patient with suspected HTN. Evaluation focuses on determining possible causes of and/or comorbidities associated with HTN. Evaluation, as is detailed in the following sections, should include appropriate patient history, family history, physical examination, laboratory evaluation, and imaging. A complete physical examination may provide clues to potential secondary causes of HTN and assess possible hypertensive end organ damage. The child's height, weight, calculated BMI, and percentiles for age should be determined at the start of the physical examination. Poor growth may indicate an underlying chronic illness. The purpose of the laboratory evaluation is to identify underlying secondary causes of HTN. Approximately one-half of adolescents with HTN have undergone electrocardiography at least once as an assessment for LVH. Echocardiography was identified in the Fourth Report as a tool to measure left ventricular (LV) target organ injury related to HTN in children. Emerging data demonstrate an association of higher levels of BP in youth with adverse changes in measures of vascular structure and function, including ultrasonography of the cIMT, PWV, a robust measure of central arterial stiffness66 that is related to hard CV events in adults. There are no evidence-based criteria for the identification of children and adolescents who may be more likely to have RAS. Some experts will do a more extensive evaluation for RAS in children and adolescents with stage 2 HTN, those with significant diastolic HTN.

Keywords: children, hypertension

Introduction

1. Patient Evaluation

As with any medical condition, appropriate diagnostic evaluation is a critical component in the evaluation of a patient with suspected HTN. Evaluation focuses on determining possible causes of and/or comorbidities associated with HTN. Evaluation, as is detailed in the following sections, should include appropriate patient history, family history, physical examination, laboratory evaluation, and imaging.

2. History

The first step in the evaluation of the child or adolescent with elevated BP is to obtain a history. The various components of the history include the perinatal history, past medical history, nutritional history, activity history, and psychosocial history. Each is discussed in the following sections.

a. Perinatal History

As discussed, perinatal factors such as maternal HTN and low birth weight have been shown to influence later BP, even in childhood.**(Staley et al., 2015)** Additionally, a high incidence of preterm birth among hypertensive children has recently been reported in 1 large case series. Thus, it is appropriate to obtain a history of pertinent prenatal information, including maternal pregnancy complications; gestational age; birth weight; and, if pertinent, complications occurring in the neonatal nursery and/or ICU. It is also appropriate to document pertinent procedures, such as umbilical catheter placement.

b. ***Nutritional History***

High sodium intake has been linked to childhood HTN and increased LVMI and is the focus of several population health campaigns.**(Daniels et al., 1990)** In NHANES 2003–2008, among children 8 to 18 years of age **(*n* = 6235)**, higher sodium intake **(as assessed by dietary recall)** was associated with a twofold increase in the combined outcome of elevated BP or HTN. The effect was threefold among participants with obesity.**(Yang et al., 2012)** Limited data suggestthe same effect is seen in younger children.**(He and MacGregor, 2006)** One study found that high intake of total fat and saturated fat, as well as adiposity and central obesity, were also predictors of SBP.**(Niinkoski et al., 2009)** Nutrition history is an important part of the patient assessment because it may identify dietary contributors to HTN and detect areas in which lifestyle modification may be appropriate. The important components to discuss include salt intake **(including salt added in the kitchen and at the table and sodium hidden in processed and fast food)**, consumption of high-fat foods, and consumption of sugary beverages **(Adler et al., 2014)** Infrequent consumption of fruits, vegetables, and low-fat dairy products should also be identified.

c. Physical Activity

History A detailed history of physical activity and inactivity is an integral part of the patient assessment, not only to understand contributors to the development of HTN but also to direct lifestyle modification counseling as an important part of management **(Cai et al., 2014)**.

d. Psychosocial History

Providers should obtain a psychosocial history in children and adolescents with suspected or confirmed HTN. Adverse experiences both prenatally **(Van Dijk et al., 2012)**and during childhood **(including maltreatment, early onset depression, and anxiety)** are associated with adult-onset HTN.**(Halonen et al., 2015)** The identification of stress may suggest a diagnosis of WCH. The psychosocial history should include questions about feelings of depression and anxiety, bullying, and body perceptions. The latter is particularly important for patients with overweight or obesity because ~70% of these children report having bullying and body perception concerns. Starting at 11 years of age, the psychosocial history should include questions about smoking,**(Yun et al., 2015)**alcohol, and other drug use.**(Hagan and Duncan, 2008)**

e. Family History

Taking and updating the family history is a quick and easy way to risk-stratify pediatric patients with an increased risk for HTN. It is important to update the family history for HTN over the course of the pediatric patient's lifetime in the practice **(typically until 18–21 years of age)** because first- and seconddegree relatives may develop HTN during this time. All too often, the diagnosis of HTN in the pediatric patient stimulates the collection of a detailed family history of HTN, sometimes even years after the pediatric patient has had elevated BP, instead of the other way around **(Benson et al., 2010)**.

TABLE 1: Family and clinical history

Family history • Hypertension • Diabetes • Dyslipidemia • Cardiovascular disease • Hereditary renal disease (polycystic kidney disease and Alport syndrome) • Hereditary endocrine disease (adrenal tumors, glucocorticoid-remediable aldosteronism, multiple endocrine neoplasia type 2 and monogenic syndromes of hypertension) • Syndromes associated with hypertension (neurofibromatosis)	**Clinical history** • Age at presentation • Previous blood pressure measurements • Past and current treatment • Compliance-adverse effects **History or symptoms of secondary hypertension** **Perinatal history:** • oligohydramnios • anoxia • umbilical artery catheterization and renal artery/vein thrombosis **Underlying or concurrent diseases** **Renal or urologic disease** • trauma • recurrent urinary tract infections, • edema, • weight loss • failure to thrive • thirst/polyuria • nocturia • hematuria **Cardiac, endocrine, or neurological disease** • cold extremities • intermittent claudication • palpitations • sweating • fever • pallor • flushing • muscle weakness, crumbs • virilization, primary amenorrhea, male pseudo-hermaphroditism **Skin abnormalities** **Systemic disease** (lupus erythematosus) **Drug/substance intake:** • Steroids • calcineurin inhibitors • TCAs • decongestants • oral contraceptives amphetamines and cocaine
Risk factors • Diabetes mellitus • Dyslipidemia • Obesity and growth patterns • Physical exercise • Dietary habits • Smoking and alcohol • Birth weight and gestational age • Snoring and sleep apnea history	
History or symptoms of target organ damage • Headache • Epistaxis • Vertigo • visual impairment • facial palsy • seizures • strokes • low school performance • dyspnea • chest pain • palpitationssyncope	

(Lurbe et al., 2016)

3. Physical Examination

A complete physical examination may provide clues to potential secondary causes of HTN and assess possible hypertensive end organ damage. The child's height, weight, calculated BMI, and percentiles for age should be determined at the start of the physical examination. Poor growth may indicate an underlying chronic illness. At the second visit with confirmed elevated BP or stage 1 HTN or the first visit with confirmed stage 2 HTN, BP should be measured in both arms and in a leg. Normally, BP is 10 to 20 mm Hg higher in the legs than the arms. If the leg BP is lower than the arm BP, or if femoral pulses are weak or absent, coarctation of the aorta may be present. Obesity alone is an insufficient explanation for diminished femoral pulses in the presence of high BP. The remainder of the physical examination should pursue clues found in the history and should focus on body systems and findings that may indicate secondary HTN and/ or end organ damage related to HTN **(Flynn et al., 2001)** The physical examination in hypertensive children is frequently normal except for the BP elevation. ***2017 AAP Guidelines recommended that****:* In children and adolescents being evaluated for high BP, the provider should obtain a perinatal history, appropriate nutritional history, physical activity history, psychosocial history, and family history and perform a physical examination to identify findings suggestive of secondary causes of HTN **(grade B, strong recommendation)**.

Table 2: Examples of Physical Examination Findings and History Suggestive of Secondary HTN or Related to End Organ Damage Secondary to HTN

Body System	Finding, History	Possible Etiology
Vital signs	Tachycardia	Hyperthyroidism
		PCC
		Neuroblastoma
	Decreased lower extremity pulses; drop	Coarctation of the aorta
	in BP from upper to lower extremities	Hyperthyroidism
Eyes	Proptosis	Severe HTN, more likely to be associated
	Retinal changes[a]	with secondary HTN
Ear, nose, throat	Adenotonsillar hypertrophy	SDB
	History of snoring	Sleep apnea
	Growth retardation	Chronic renal failure
Height, weight	Obesity (high BMI)	Cushing syndrome
	Truncal obesity	Insulin resistance syndrome
Head, neck	Elfin facies	Williams syndrome
	Moon facies	Cushing syndrome
	Thyromegaly, goiter	Hyperthyroidism
	Webbed neck	Turner syndrome
Skin	Pallor, flushing, diaphoresis	PCC
	Acne, hirsutism, striae	Cushing syndrome
		Anabolic steroid abuse
	Café-au-lait spots	Neurofibromatosis
	Adenoma sebaceum	Tuberous sclerosis
	Malar rash	Systemic lupus
	Acanthosis nigricans	T2DM

Hematologic	Pallor Sickle cell anemia	Renal disease
Chest, cardiac	Chest pain Palpitations Exertional dyspnea Widely spaced nipples Heart murmur Friction rub Apical heave[a]	Heart disease Turner syndrome Coarctation of the aorta Systemic lupus (pericarditis) Collagen vascular disease LVH
Abdomen	Abdominal mass Epigastric, flank bruit Palpable kidneys	Wilms tumor Neuroblastoma PCC RAS Polycystic kidney disease Hydronephrosis Multicystic dysplastic kidney
Genitourinary	Ambiguous or virilized genitalia Urinary tract infection Vesicoureteral reflux Hematuria, edema, fatigue	Congenital adrenal hyperplasia Renal disease
Extremities	Joint swelling Muscle weakness	Systemic lupus Collagen vascular disease
Neurologic, metabolic	Hypokalemia, headache, dizziness, polyuria, nocturia Muscle weakness, hypokalemia	Hyperaldosteronism Liddle syndrome Reninoma Monogenic HTN (Liddle syndrome, GRA, AME)

4. Laboratory Evaluation

The purpose of the laboratory evaluation is to identify underlying secondary causes of HTN **(eg, renal or endocrine disease)** that would require specific treatment guided by a subspecialist. In general, such testing includes a basic set of screening tests and additional, specific tests; the latter are selected on the basis of clues obtained from the history and physical examination and/or the results of the initial screening tests.**(Wiesen et al., 2008)** This table provides a list of screening tests and the populations in which they should be performed.

Table 3: Screening tests and relevent population.

Patient Population	Screening Tests
All patients	Urinalysis Chemistry panel, including electrolytes, blood urea nitrogen, and creatinine Lipid profile (fasting or nonfasting to include high-density lipoproteina and total cholesterol) Renal ultrasonography in those <6 y of age or those with abnormal urinalysis or renal function Hemoglobin A1c (accepted screen for diabetes)
In the obese (BMI >95th percentile) child or adolescent, in addition to the above	Aspartate transaminase and alanine transaminase (screen for fatty liver) Fasting lipid panel (screen for dyslipidemia) Fasting serum glucose for those at high risk for diabetes mellitus Thyroid-stimulating hormone
Optional tests to be obtained on the basis of history, physical examination, and initial studies	Drug screen Sleep study (if loud snoring, daytime sleepiness, or reported history of apnea) Complete blood count, especially in those with growth delay or abnormal renal function

5. Electrocardiography

Approximately one-half of adolescents with HTN have undergone electrocardiography at least once as an assessment for LVH **(Yoon et al., 2012)** Unlike echocardiography, electrocardiography takes little time and is a relatively low-cost test. Electrocardiography has high specificity but poor sensitivity for identifying children and adolescents with LVH. **(Ramaswamy et al., 2009)** ***2017 AAP Guidelines recommended that***: The positive predictive value of electrocardiography to identify LVH is extremely low.**(Grossman et al., 2012)** children and adolescents being evaluated for LVH **(grade B, strong recommendation) (Flynn et al., 2017).**

6. Imaging Evaluation, Echocardiography: Detection of Target Organ Damage

Echocardiography was identified in the Fourth Report as a tool to measure left ventricular **(LV)** target organ injury related to HTN in children.1 The basis for this assessment is as follows: **(1)** the relationship of LV mass to BP,**(Urbina et al., 1995)(2)** the independent and strong relationship of LVH to adverse CVD outcomes in adults,**(Armstrong et al., 2014)** and **(3)** that a significant percentage of children and adolescents with HTN demonstrate the degree of LVH associated with adverse outcomes in adults.**(Gidding et al., 2014)** Antihypertensive treatment reduces LVH. Observational data suggest that the regression of LVH independently predicts outcomes in adults **(Devereux et al., 2004)** The best-studied measures of LV target organ injury are measures of LV structure **(LV mass and the relationship of LV wall thickness or mass to LV cavity volume)** and systolic function **(LV ejection fraction)**. LV structure is usually stratified into 4 groups on the basis of LV mass **(normal or hypertrophied)** and relative LV wall thickness **(normal or increased)**. These 4 are as follows: **(1)** normal geometry with normal LV mass and wall thickness, **(2)** concentric geometry with normal LV mass and increased LV wall thickness, **(3)** eccentric LVH with increased LV mass and normal LV wall thickness, and **(4)** concentric LVH with both increased LV mass and increased relative wall thickness.**(Lang et al., 2015)**

The American Society of Echocardiography recommendations should be followed with regard to image acquisition and LV measurement for calculating LV ejection fraction, mass, and relative wall thickness **(Lopez et al., 2010)**. LV ejection fraction may be significantly decreased in severe or acute onset HTN with associated congestive heart failure. Rarely, LV ejection fraction may be mildly depressed in chronic HTN. Because the heart increases in size in relation to body size, indexing LV mass is required. Indexing LV mass is particularly important in infants and younger children because of their rapid growth. **(Foster et al., 2016)**

Physical training increases LV mass in a healthful manner. Lean body mass is more strongly associated with LV mass than fat mass. Because body composition is not routinely measured clinically, surrogate formulae for indexing are required. It is unclear whether expected values for LV mass should be derived from reference populations of normal weight and normotensive children or should include normotensive children who have overweight or obesity. The best method for indexing LV mass in children is an area of active investigation. For this document, the following definitions for LV target organ injury have been chosen regarding hypertrophy, relative wall thickness, and ejection fraction. These definitions are based on published guidelines from the American Society of Echocardiography and associations of thresholds for indexed LV mass with adverse outcomes in adults**(Lang et al., 2015)** LVH is defined as LV mass >51 g/m2.7 or LV mass >115 g per body surface area **(BSA)** for boys and LV mass >95 g/BSA for girls. **(Note that the values for LVH are well above the 95th percentile for distributions of LV mass in children and adolescents (Lang et al., 2015)**

The clinical significance of values between the95th percentile of a populationbased distribution and these thresholds is uncertain372) An LV relative wall thickness >0.42 cm indicates concentric geometry. LV wall thickness >1.4 cm is abnormal **(Khoury et al., 2009)**; Decreased LV ejection fraction is a value <53%. There are a number of additional evidence gaps related to the echocardiographic assessment of LV target organ injury. The value of LV mass assessment in risk reclassification independent of conventional risk assessment has not been established in adults **(Armstrong et al., 2014)** The costs and benefits of incorporation of echocardiography into HTN care has not been assessed. Quality control regarding reproducibility of measurements across laboratories may be suboptimal **(Lipshultz et al., 2001)**

The most accurate method to measure LV mass **(M-mode; two-dimensional; or, in the near future, three-dimensional techniques)** requires further research. *2017 AAP Guidelines recommended that15* 1. It is recommended that echocardiography be performed to assess for cardiac target organ damage **(LV mass, geometry, and function)** at the time of consideration of pharmacologic treatment of HTN; 2. LVH should be defined as LV mass >51 g/m2.7 **(boys and girls)** for children and adolescents older than 8 years and defined by LV mass >115 g/BSA for boys and LV mass >95 g/BSA for girls; 3. Repeat echocardiography may be performed to monitor improvement or progression of target organ damage at 6- to 12-month intervals. Indications to repeat echocardiography include persistent HTN despite treatment, concentric LV hypertrophy, or reduced LV ejection fraction, ***2017 AAP Guidelines recommended that***: 1. It is recommended that echocardiography be performed to assess for cardiac target organ damage (LV mass, geometry, and function) at the time of consideration of pharmacologic treatment of HTN; 2. LVH should be defined as LV mass >51 g/m2.7 (boys and girls) for children and adolescents older than 8 years and defined by LV mass >115 g/BSA for boys and LV mass >95 g/BSA for girls; 3. Repeat echocardiography may be performed to monitor improvement or progression of target organ damage at 6- to 12-month intervals. Indications to repeat echocardiography include persistent HTN despite treatment, concentric LV hypertrophy, or reduced LV ejection fraction; 3.In patients without LV target organ injury at initial echocardiographic assessment, repeat echocardiography at yearly intervals may be considered in those with stage 2 HTN, secondary HTN, or chronic stage 1 HTN incompletely treated **(noncompliance or drug resistance)** to assess for the development of worsening LV target organ injury **(grade C, moderate recommendation) (Flynn et al., 2017).**

7. Vascular Structure and Function

Emerging data demonstrate an association of higher levels of BP in youth with adverse changes in measures of vascular structure and function, including ultrasonography of the cIMT, PWV, a robust measure of central arterial stiffness66 that is related to hard CV events in adults**(eg, stroke, myocardial infarction, etc)**, and FMD, which assesses endothelial function and describes the ability of the endothelium to release nitric oxide in response to stress **(Urbina, 2016)** Although there are multiple large studies of PWV in youth, **(Lurbe et al., 2012)**. they all suffer from notable limitations, primarily the lack of racial and ethnic diversity and differences in measurement devices and protocols. Researchers in the largest study of PWV in youth to date **(*N* = 6576)** only evaluated 10 and 11 year olds and measured only carotid-radial PWV across the arm; this measure has not been linked to CV events in adults.382 Researchers in one large study of FMD performed in youth **(*N* = 5809)** only included 10- to 11-year-old children in England.**(Charakida et al., 2012)** The largest set of data for cIMT included 1155 European youth who were 6 to 18 years of age.**(Doyon et al., 2013)**

No racial and ethnic breakdown was provided for this study. The wide heterogeneity in the methods for cIMT measurement hinders the pooling of data. For instance, researchers in the aforementioned article only measured common carotid **(Doyon et al., 2013)** although the bulb and internal carotid are the sites of earliest atherosclerotic disease.**(Urbina et al., 2009)**

Many studies have had significant issues related to methodology. For example, carotid-femoral PWV is not measured identically with different devices and is not equivalent to other measures of PWV, such as brachial-femoral PWV.**(Keehn et al., 2014)** No direct comparisons have been made between carotid-femoral and brachialankle PWV, methods in which brachial-ankle PWV provide values considerably higher than carotidfemoral PWV.**(Miyai et al., 2013)**

The brachial-ankle PWV measures stiffness along both a central elastic artery **(aorta)** and the medium muscular arteries of the leg. Therefore, insufficient normative data are available to define clinically actionable cut-points between normal and abnormal for these vascular parameters. The routine measurement of vascular structure and function to stratify risk in hypertensive youth cannot be recommended at this time.

8. Imaging for Renovascular Disease

There are no evidence-based criteria for the identification of children and adolescents who may be more likely to have RAS. Some experts will do a more extensive evaluation for RAS in children and adolescents with stage 2 HTN, those with significant diastolic HTN **(especially on ABPM)**, those with HTN and hypokalemia on screening laboratories, and those with a notable size discrepancy between the kidneys on standard ultrasound imaging. Bruits over the renal arteries are also suggestive of RAS but are not always present. Consultation with a subspecialist is recommended to help decide which patients warrant further investigation and to aid in the selection of the appropriate imaging modality.

a. *Renal Ultrasonography*

The utility of Doppler renal ultrasonography as a noninvasive screening study for the identification of RAS in children and adolescents has been examined in at least 2 recent case series; sensitivity has been reported to be 64% to 90%, with a specificity of 68% to 70%.3**(Castelli et al., 2014)** In another study that included both children and adults, sensitivity and specificity for the detection of renal artery stenoses was 75% and 89%, respectively.389 Factors that may affect the accuracy of Doppler ultrasonography include patient cooperation, the technician's experience, the age of the child, and the child's BMI. Best results are obtained in older **(≥8 years)**, **(Castelli et al., 2014)** nonobese **(BMI ≤85th percentile)**, cooperative children and adolescents who are examined in a facility with extensive pediatric vascular imaging experience. Doppler ultrasonography should probably not be obtained in patients who do not meet these criteria or in facilities that lack appropriate pediatric experience. ***2017 AAP Guidelines recommended that:*** Doppler renal ultrasonography may be used as a noninvasive screening study for the evaluation of possible RAS in

normal-weight children and adolescents ≥8 years of age who are suspected of having renovascular HTN and who will cooperate with the procedure **(grade C, moderate recommendation) (Flynn et al., 2017).**

b. ***Computed Tomographic Angiography, Magnetic Resonance Angiography, and Renography***

Other noninvasive imaging studies that have been assessed for their ability to identify RAS include computed tomographic angiography **(CTA)**, magnetic resonance angiography **(MRA)**, and nuclear medicine studies. Each of thesehas been **compared with the gold standard, renal arteriography. CTA and MRA have generally been found to be acceptable as noninvasive imaging modalities for the identification of hemodynamically significant vascular stenosis. One study that included both pediatric and adult patients showed that the sensitivity and specificity for the detection of RAS was 94% and 93% for CTA and 90% and 94% for MRA, respectively.**(Rountas et al., 2007)** Unfortunately, studies of either technique that include only pediatric patients are limited at best for CTA and are nonexistent for MRA. Despite this, expert opinion holds that either modality may be used for noninvasive screening for suspected RAS, but neither is a substitute for angiography.**(Marks and Tullus, 2012)** CTA typically involves significant radiation exposure, and MRA generally requires sedation or anesthesia in young children, which are factors that must be considered when deciding to use one of these modalities. Nuclear renography is based on the principle that after the administration of an agent affecting the renin-angiotensinaldosterone system **(RAAS)**, there will be reduced blood flow to a kidney or kidney segment affected by hemodynamically significant RAS. Such reduced blood flow can be detected by a comparison of perfusion before and after the administration of the RAAS agent. Limited pediatric nuclear renography studies exist that show variable sensitivity and specificity, ranging from 48% to 85.7% and 73% to 92.3%, respectively.**(Abdulsamea et al., 2010)**

The utility of nuclear renography may be less in children then adults because children with RAS often have more complicated vascular abnormalities than adults.**(Reusz et al., 2010)**Given these issues, nuclear renography has generally been abandoned as a screening test for RAS in children and adolescents. ***2017 AAP Guidelines recommended that:*** In children and adolescents suspected of having RAS, either CTA or MRA may be performed as a noninvasive imaging study. Nuclear renography is less useful in pediatrics and should generally be avoided **(grade D, weak recommendation) (Flynn et al., 2017).**

9. Uric Acid

Cross-sectional data have suggested a relationship between elevated serum uric acid **(UA)** levels and HTN. Two recent studies of adolescents included in NHANES 1999–2000 and a small study conducted in Italy found that elevated UA levels were associated with higher BP.**(Viazzi et al., 2013)** In the Italian study and in another US study of youth with obesity and HTN, **(Reschke et al., 2015)** elevated UA was also associated with other markers of CV risk. These findings suggest that the measurement of UA levels may best be viewed as 1 component of CV risk assessment, especially in those with obesity. A causative role for elevated UA in the development of childhood HTN has not been definitively established, although recent studies suggest that it may be on the causal pathway. A longitudinal study in which researchers followed a group of children for an average of 12 years demonstrated that childhood UA levels were associated with adult BP levels even after controlling for baseline BP.**(Alper et al., 2005)** A few small, single-center clinical trials have also shown that lowering UA can decrease BP levels, and increased UA levels blunt the efficacy of lifestyle modifications on BP control.**(Assadi, 2014)** No large-scale, multicenter study has yet been conducted to confirm these preliminary findings. Hence, there is currently not sufficient evidence to support the routine measurement of serum UA in the evaluation and management of children with elevated BP.

10. Microalbuminuria

Microalbuminuria **(MA)**, which should be differentiated from proteinuria in CKD, has been shown to be a marker of HTN-related kidney injury and a predictor of CVD in adults **(Flynn et al., 2017)** MA has been shown to be effectively reduced via the use of ARBs and ACE inhibitors in adults. Lowering the degree of MA in adults has been associated with decreased CVD risk. In contrast, data to support a clear relationship between HTN and MA in pediatric patients with primary HTN are limited **(Tsioufis et al., 2011)** A single, retrospective study of children with primary HTN and WCH found that 20% of the former had MA versus 0% of the latter. MA appears to be a nonspecific finding in children that can occur in the absence of HTN; it can occur in children who have obesity, insulin resistance, diabetes, dyslipidemia, and even in those who have recently participated in vigorous physical activity.**(Sanad and Gharib, 2011)**
The previously mentioned study by **(Seeman et al., 2012)** did not control for these potential confounders. Limited, single-center data suggest that a reduction in the degree of MA, more than a reduction in BMI or SBP, is associated with a decrease in LVMI. In particular, researchers in this single-center, nonrandomized, prospective study of 64 hypertensive children without kidney disease who were 11 to 19 years of age evaluated the children at baseline and after 12 months of combination ACE and hydrochlorothiazide **(*N* = 59)** or ACE, hydrochlorothiazide, and ARB therapy **(*N* = 5)**. Results found that lowering MA in children is associated with a regression of LVH **(Assadi, 2007)** Given the single-center design and lack of a control group, however, the applicability of these findings to the general population of children with primary HTN is unknown. ***2017 AAP Guidelines recommended that:*** Routine testing for MA is not recommended for children and adolescents with primary HTN **(grade C, moderate recommendation) (Flynn et al., 2017).**

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