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Detection of Early Diastolic Alterations by Tissue Doppler Imaging in Untreated Childhood-Onset Essential Hypertension

Ngozi C. Agu, MD^a, Karen McNiece Redwine, MD, MPH^{b,c}, Cynthia Bell, M.S^c, Kathleen Marie Garcia, RDCS^d, David S. Martin, MS, RDCS^d, Tim S. Poffenbarger^c, John T. Bricker, MD^a, Ronald J. Portman, MD^c, and Monesha Gupta-Malhotra, MBBS^{a,b}

^aDivision of Pediatric Cardiology, Department of Pediatrics, Children's Memorial Hermann Hospital, The University of Texas Medical School, Houston, Texas

^bDivision of Pediatric Nephrology, Department of Pediatrics, Children's Hospital of Arkansas, University of Arkansas for Medical Sciences, Little Rock, Arkansas

^cDivision of Pediatric Nephrology, Department of Pediatrics, Children's Memorial Hermann Hospital, The University of Texas Medical School, Houston, Texas

^dWyle Science, Technology and Engineering, Cardiovascular Laboratory at National Aeronautics and Space Administration Johnson Space Center, Houston, Texas

Abstract

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Corresponding Author: Monesha Gupta, MBBS, FAAP, FACC, FASE, Division of Pediatric Cardiology, Children's Memorial Hermann Hospital, University of Texas, Houston Medical School, 6410 Fannin Street, UTPB Suite 425, Houston, TX 77030, Tel: 713 500 5743, Fax: 713 500 5751, Monesha.gupta@uth.tmc.edu.

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Background—Aim of the study was to determine the presence of preclinical diastolic dysfunction in hypertensive children relative to normotensive children by Tissue Doppler Imaging (TDI).

Methods—We prospectively enrolled children with untreated essential hypertension in absence of any other disease and a matched healthy control group with normal blood pressure (BP); both groups confirmed by clinic BP and a 24 hour ambulatory BP monitoring. Echocardiographic diastolic parameters were determined using spectral transmitral inflow Doppler, flow propagation velocity, TDI, and systolic parameters were determined via midwall shortening fraction and ejection fraction.

Results—A total of 80 multiethnic children were prospectively enrolled for the study: 46 hypertensive (median age 13 years, 72% males) and 34 control (median age 14 years, 65% males). The only echocardiography parameters which had a statistically significant change compared to the control children, were regional mitral Ea, Aa and the E/Ea ratio by TDI. In comparison to controls, hypertensive children had lower Ea and Aa velocities of anterior and posterior walls and higher lateral wall E/Ea ratio. The decrease in posterior wall Ea and Aa remained significant after adjustment for gender, age, body mass index, ethnicity, and left ventricular hypertrophy on multivariate analysis. The lateral and septal wall E/Ea ratios correlated significantly with fasting serum insulin levels on similar multivariate analysis.

Conclusions—Decreased regional TDI velocities were seen with preserved left ventricular systolic function even when other measures of diastolic dysfunction remained unchanged in untreated hypertensive children. Hypertension and serum insulin levels had strong associations with preclinical diastolic alterations in children.

Keywords

Echocardiography; hypertension; pediatrics; insulin; diastole

Introduction

Childhood-onset essential hypertension has an unknown prevalence, although prevalence of hypertension in children in general is reported at 3.2% to 13% (1-3) in various studies in the United States. Interestingly, childhood hypertension is associated with target organ damage including cardiovascular changes such as changes in left ventricular geometry and left ventricular hypertrophy (4-7), increase in carotid intima-media thickness(6) and decrease in arterial compliance(8); all harbingers of chronic heart failure and premature atherosclerosis. Hence, early detection and treatment of hypertension heart disease in children is important for prevention of future complications.

Diastolic dysfunction occurs with myocardial fibrosis and ischemia in chronic systemic hypertension and with increasing age. This left ventricular diastolic dysfunction with a restriction in the left ventricular filling is a hallmark of hypertensive heart disease. In adults, mitral valve annular spectral Tissue Doppler Imaging (TDI) has been used as a reliable non-invasive surrogate marker of raised left ventricular diastolic pressure and also a predictor for cardiac death from heart failure (9). Although, diastolic impairment has been well demonstrated in hypertensive adults; few studies have been done in hypertensive children (8,

10-13). Previous studies showing diastolic impairment by TDI in hypertensive children have focused predominantly on populations of children with high rates of Caucasian ethnicity(8, 14) or African American ethnicity(12), obesity (8, 12, 14) and type II diabetes (8). Furthermore, in children, left ventricular diastolic dysfunction has been demonstrated in the absence of hypertension, in conditions such as type 2 diabetes(15) and obesity(16). Thus in children with hypertension, it becomes important to evaluate for diastolic dysfunction to differentiate from other related conditions such as athlete's heart, insulin resistance or obesity.

We hypothesized that children with uncomplicated essential hypertension are unlikely to have presentations of systolic or diastolic heart failure in childhood or demonstrate an increase in the left atrial volume (14) but may show signs of early diastolic impairment that could be useful clinically. Our aim was to prospectively evaluate left ventricular diastolic function using a sensitive and specific noninvasive tool such as TDI, among multiethnic, non-diabetic, untreated hypertensive children. We evaluated healthy normotensive children matched for gender, age and body size for comparison. The hypertensive and normotensive status in each group was confirmed by a 24-hour ambulatory blood pressure monitoring.

Methods

Institutional Approval

The protocol was approved by a Committee for the Protection of Human Subjects at the University of Texas Health Science Center and by the Johnson Space Center Committee for the Protection of Human Subjects. All subjects and parents gave informed assent and consent, respectively for this study. We were careful to maintain full patient confidentiality, safeguard the rights and welfare of human subjects, and inform subjects in a confidential manner of the results of the study.

Patient Population

This was a prospective case-control study of subjects aged 5 to 19 years who had history of hypertension matched to healthy controls with similar body size for age and gender. We did not know the duration of hypertension before diagnosis in these children but all children were enrolled before they received any therapy. Hypertensive pediatric subjects consisted of: (1) *Referral Study Population*: patients referred to the hypertension program after detection of elevated blood pressure (BP) by a primary care provider, and (2) *Recruited Study Population*: patients identified by systematic school-based screening for hypertension in students aged 11 to 18 years in Houston area public schools. Parents are notified in advance by a letter sent from each school about the screening program. Forms were provided for parents to sign and return if they did not wish their child to participate. At each screening, three seated BP measurements were made at least 1 minute apart using oscillometric monitors. Students found to have an average BP above the 95th percentile BP (17) value specific for their gender, age and height-percentile underwent a second set of BP measurements 1-2 weeks later. Students found to have BP above the 95th percentile at the second screening underwent a third set of BP measurements an additional 1-2 weeks later. Students with elevated BP on all 3 occasions were considered to be hypertensive. Families

of hypertensive children are informed of the persistent BP elevation and invited to participate in a clinic-based study of hypertensive end-organ injury in children. *Inclusion criteria:* Criteria for inclusion in further analysis were: 1) casual BP elevation above the 95th percentile on 3 previous occasions, and 2) no concurrent medication with the potential to raise BP (such as prednisone or methylphenidate). Demographic and anthropometric data were collected on all subjects at study entry. Patients recruited by these 2 methods that is, school screening and referral, as described above have previously been shown to be similar(18). Because normative data for TDI is lacking in children, we recruited, via advertisement, age- and gender-matched healthy children serving as controls from the general population. Both, control and patient population were remunerated for their participation in this study and all evaluation, including ambulatory BP monitoring (ABPM) and an echocardiogram, were done without any charge to the recruited population.

BP Protocol

All subjects, including control population, underwent casual BP measurements and evaluation of their ambulatory BP for 24 hours as part of their evaluation protocol. The children along with their families were instructed upon avoidance of caffeinated medications, any medications or over the counter products, smoking and alcohol for 24 hours prior to the study. BP was measured as follows *Casual BP:* Casual hypertensive status was confirmed in all subjects at the first visit to the hypertension clinic by averaging the last three of the four BP measurements (manual auscultation with a mercury sphygmomanometer) taken by trained personnel using methodology recommended by the Fourth Working Group (17). Manual auscultatory measurements were used for analysis of clinic BP (17). *Ambulatory BP Monitoring:* All subjects above 5 years of age underwent ambulatory BP monitoring (ABPM) using Spacelabs oscillometric monitors (Spacelabs, Inc., Redmond, WA). Blood pressure was measured every 20 minutes for 24 hours. Only subjects with casual hypertension confirmed with 24-hour systolic BP or diastolic BP greater than the pediatric 95th percentile or BP load (percentage of BP values exceeding the 95th percentile for the 24-hour period) greater than 25% were considered hypertensive. Subjects with casual hypertension but with 24-hour systolic BP and diastolic BP less than the pediatric 95th percentile and BP load less than 25% were considered to have white coat hypertension and were excluded. Control subjects were those without evidence of casual hypertension along with a 24-hour systolic BP and diastolic BP less than the pediatric 95th percentile and BP load less than 25% were considered to be normotensive. If subjects had evidence of White Coat Hypertension or prehypertension, they were excluded from the study. Once hypertension was confirmed by ABPM, all subjects underwent further evaluation for secondary causes of hypertension in a standard manner, including a renal ultrasound and a transthoracic echocardiogram before therapy. The control population included those children who had a normal evaluation by casual measures and by ABPM and they underwent laboratory testing and a transthoracic echocardiogram in the same manner as study children.

Echocardiography Protocol

Studies were performed and measurements made in a blinded manner on all patients regardless of their hypertension status by two research sonographers (KMG, DSM) from the

National Aeronautics and Space Administration and Wyle Science Technology and Engineering Group using a transthoracic echocardiogram machine (ATL HDI 5000 CV ultrasound, Philips Medical Systems, Bothell, Washington, USA), via a standard pediatric protocol to rule out congenital heart disease and to assess function by means of various parameters(19). The studies were acquired and recorded both digitally and on a super VHS videocassette for later review. All studies were evaluated by two cardiologists (NA, MGM) for the various parameters and for presence of congenital heart disease, including bicuspid aortic valve and coarctation of the aorta. Those found to have congenital cardiac disease including bicuspid valves were excluded from this study.

Detailed assessments of left ventricular systolic and diastolic function were made using transthoracic echocardiography per protocol (20). An average of 3 measurements in different cardiac cycles were made of mitral valve inflow velocities in the four-chamber view, including early (E) and late (A) filling using spectral pulse Doppler. TDI via spectral Doppler (figure 1) were made from apical views were performed ensuring minimal incidence angle between the Doppler beam and the plane of the mitral annulus movement. Since TDI evaluation in hypertensive children is limited, we sought to measure the values of all the walls of the left ventricle, in both longitudinal and radial planes. Thus, TDI evaluation included early (Ea) and late (Aa) filling at different parts of the mitral valve annulus - lateral and septal (from the apical four-chamber view), posterior (from the apical long axis), anterior and inferior (from the apical two-chamber view) and radial (from the parasternal long axis view). The correlation coefficients for intraobserver and interobserver were 0.98 and 0.94, respectively. Color M-mode Doppler flow propagations velocities (Vp) were obtained of left ventricular inflow from the apical four-chamber view using the slope method (figure 2) (21). The M-mode measurements for Vp were made at the center of the left ventricular inflow from the mitral valve to the apex and 6 measurements were made and averaged.

M-mode measurements obtained during diastole by means of transthoracic echocardiography included intraventricular septal thickness, left ventricular end-diastolic dimension, and posterior wall thickness. Left ventricular mass was calculated according to Working Group recommendations using the equation of Devereux et al(22) with measurements (in cm) obtained by criteria of the American Society of Echocardiography (23). LVMI was calculated by dividing LVM by $height^{2.7}$ to minimize effects of age, gender, ethnicity, and overweight status.(24-26) The left ventricle geometry was determined using a relative wall thickness cut off of 0.42(27).

Laboratory Data

All patients underwent standard evaluation for diagnosis of primary hypertension including evaluation for renal artery stenosis by a magnetic resonance imaging and catecholamine secreting tumors and so on (17). The children without any detectable secondary cause of hypertension were labeled with essential hypertension. Laboratory data evaluation included among others, assessment for renal dysfunction, thyroid disease and for co-morbid conditions including fasting serum cholesterol, low and high density lipoprotein, triglycerides, insulin and glucose.

Statistics

Continuous outcome measures were compared using Wilcoxon Rank-Sum tests and reported as mean ($\pm$ standard deviation). All categorical variables were tested using two-tailed Fisher's Exact tests and reported as count (%). Type I error rate was set at 0.05 and all tests were two-sided. Although we had a larger Caucasian population in the control group, the race-ethnicity differences in diastolic function were attenuated in multivariate models that included age, gender, body mass index, race and left ventricular hypertrophy. Due to high correlation within cardiovascular and laboratory variables, predictor variables were tested for correlation by Pearson's correlation coefficient, Fishers Exact test or Rank-Sum test before inclusion in a multivariate model. Multivariate models were restricted to non-correlated predictor variables to maintain the assumption of independence.

Results

A total of 80 children with untreated systemic hypertension and their healthy controls between 6 and 17 years of age were prospectively enrolled for the study (Table 1). The normotensive children had BPs $<90^{\text{th}}$ percentile based on their clinic measurements and confirmed by a 24-hour ambulatory BP monitoring. The ethnicities of normotensive children were: African American 2 (6%), Caucasian 20 (59%), and Hispanic 12 (35%). The hypertensive children had BPs $>95^{\text{th}}$ percentile based on their clinic measurements and confirmed by a 24-hour ambulatory BP monitoring. The ethnicities of hypertensive children were: African American 15 (33%), Caucasian 15 (33%), Hispanic 15 (33%) and Asian 1 (1%).

The 46 hypertensive children had significantly increased left ventricular mass and abnormal left ventricular geometry relative to their matched controls (Table 2). Of note, amongst them, 25 (54%) had left ventricular hypertrophy as follows: 14 (56%) had eccentric left ventricular hypertrophy 11 (44%) had concentric left ventricular hypertrophy. None of the control children had left ventricular hypertrophy.

Evaluation of the left ventricular systolic function (Table 2) using ejection fraction, fractional shortening, and midwall fractional shortening showed no significant difference between the cases and controls. Evaluation of the left ventricular diastolic function (Table 2) using measures of mitral valve inflow spectral Doppler and velocity of propagation (Vp) by color M-mode showed no significant difference between the cases and controls. However, diastolic function evaluation using myocardial TDI parameters of early filling velocities and late filling velocities at the anterior and posterior walls were significantly decreased in the hypertensive group relative to the matched controls (Table 2); also confirmed for posterior wall on multivariate analysis after adjustment for gender, age, body mass index percentile, race/ethnicity and left ventricular hypertrophy (Table 4).

While there were no differences found between hypertensive and normotensive children in laboratory data, including lipid profile and glucose (Table 3); on univariate and on multivariate analysis after adjustment for gender, age, body mass index percentile, race/ethnicity and left ventricular hypertrophy (Table 4), serum insulin levels were significantly correlated with E/Ea ratios of the lateral and septal walls.

Discussion

Diastolic dysfunction in hypertensive patients presents as a continuum progressing from impaired left ventricular filling to elevated end diastolic pressure, elevated left atrial and pulmonary capillary wedge pressure and finally to signs of pulmonary congestion(28, 29). This progression is more clearly demonstrated in adults; however in children the diagnosis of diastolic dysfunction remains a challenge (30). We studied non-diabetic, untreated hypertensive children of major ethnicities using various echocardiographic parameters in order to detect subclinical changes that would be consistent with diastolic impairment in this population. Since normative data or reference standard on TDI values in children are sparse and found to be related to age and cardiac growth(31) (32), we sought to age-, gender- and size-match our hypertensive children to controls.

Our prospectively conducted study of a multiethnic population of well characterized hypertensive children prior to antihypertensive therapy demonstrated preserved echocardiographic measures of left ventricular systolic function (measured by ejection fraction, shortening fraction and midwall shortening fraction) and diastolic function (measured by transmitral spectral Doppler and flow propagation velocities by color M-mode) relative to matched control children without hypertension. However, on univariate analysis there was a significantly decreased (although not below normal(31)) Doppler velocities of mitral valve annular tissue in the anterior and posterior wall and increase in lateral and septal wall E/Ea ratios in hypertensive children relative to controls, indicating early regional abnormalities in diastole in response to untreated hypertension. In adults, the septal wall E/Ea ratios have been found to reliably estimate the left ventricular diastolic pressure in presence of preserved left ventricular systolic function and an increase in septal E/Ea ratio is a hallmark of functional disability in several clinical settings (33).

On a multiple regression model the regional diastolic alterations by TDI in our hypertensive children remained significant after controlling for gender, age, body-mass index percentile, ethnicity and left ventricular hypertrophy. Thus, the indicators of diastolic alterations as characterized by decreased mitral annulus Ea and Aa waves (relaxation indices) and increased E/Ea ratio (compliance indices) in adults, although not validated in children, were also seen in certain cardiac segments in our hypertensive children relative to controls. The variation in TDI velocities between the various left ventricular myocardial walls in our patients may be attributable to the heterogeneity of the myofiber orientation and relaxation abilities. It is important to note that alternative method to TDI for estimating left ventricular filling pressure such as E/Vp remained unchanged in our study population. Furthermore, there was a trend for increased radial function by TDI in the hypertensive children which might be anticipated from other studies in similar circumstances in adults related to change in shape of the ventricles, although the trend did not reach a statistical significance possibly due to the small sample size. Although these preclinical regional diastolic alterations are mild at this stage of early untreated essential hypertension and do not indicate diastolic failure; they could certainly evolve into hypertensive heart disease with age.

The myocardial mechanics change from fetal life into adulthood. Due to its high temporal resolution and decreased sensitivity to preload(34), multiple investigators have used TDI as

a non-invasive tool for tracking tissue motion to advance the understanding of cardiac growth and pathophysiology. We found that in comparison to adults, the overall Ea values were much higher in all children, both in hypertensive and normotensive groups. The myocardial tissue velocities (Ea) as assessed by TDI increase with growth during childhood and the changes and show regional variations (31, 32). In a multiple regression analysis, the mitral valve Ea velocities have been shown to have a strong positive correlation with age in children (31). It appears from our study that these velocities may later start to decrease from childhood into adulthood.

Our study also demonstrated an increase in left ventricular mass and a higher likelihood of development of abnormal left ventricular geometry in children who had essential hypertension; eccentric hypertrophy being the most prevalent type of abnormal geometry (35). According to the literature in children, a high incidence of concentric hypertrophy is seen in the obese and hypertensive children (12, 36) and it is also the type that is less likely to regress (35). Left ventricular hypertrophy is the most commonly assessed marker of target organ damage in hypertensive children with a prevalence of 10% to 38% (6, 7, 11, 36-41) and is a significant independent predictor of diastolic dysfunction in children with essential hypertension (14). However, in children left ventricular hypertrophy is not only associated with hypertensive heart disease but can be due to many other causes, including steroid use, growth hormone use(42), obesity(43, 44) and insulin resistance(44, 45). Furthermore, left ventricular hypertrophy is not always indicative of disease and can be seen in athletes without diastolic impairment; in fact the diastolic function improves with athletic training (46, 47). In our study, the regional diastolic abnormalities in the hypertensive children continued to be significant after adjusting for left ventricular hypertrophy in a multiple regression analysis.

Furthermore, in our multiethnic non-diabetic children, we found that the regional decrease in compliance (decrease in E/Ea ratios of the lateral and septal walls) correlated significantly with serum insulin levels on multivariate analysis. In adults, diastolic dysfunction as demonstrated by impaired left ventricular relaxation has been shown to correlate with serum insulin levels (48). In diabetic cardiomyopathy, impaired left ventricular relaxation has been found to be the earliest indicator of myocardial involvement (49, 50) and has been demonstrated in children as well (15). These findings indicate that insulin may play a role in the development of cardiomyopathy in hypertensive children.

Limitations

We did not evaluate our patient population by other advanced methodologies such as transthoracic strain imaging and 3-dimensional imaging or cardiac magnetic resonance imaging. Since pulmonary veins velocities do not add information to the methods already used for evaluation of diastolic dysfunction in our study, we did not assess the pulmonary vein velocities (20). This study had all the limitations in the power due to limited sample size. We also lacked longitudinal follow-up data of these children. We recommend a multicenter trial with a sufficiently large sample size to study the diastolic changes in hypertensive children and other factors, such as hyperinsulinemia, contributing to these changes.

Conclusions

Early regional diastolic alterations with preserved left ventricular systolic function can be demonstrated by tissue Doppler imaging in childhood-onset essential hypertension prior to antihypertensive therapy even when other conventional measures of diastolic function such as transmitral Doppler and flow propagation velocity remain unchanged. Hypertension and serum insulin levels have strong associations with these early diastolic alterations. Our findings indicate the importance of tissue Doppler imaging for earlier detection of subclinical cardiomyopathy due to hypertension.

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Figure 1. Spectral Tissue Doppler Imaging showing the variables measured including the left ventricular intraventricular contraction time (IVCT), ejection times (ET), systolic (S), early (E) and late (A) diastolic filling velocities in a hypertensive child

Figure 2.
Color M-Mode of mitral valve inflow showing the velocity of propagation made at the center of the left ventricular inflow from the mitral valve to the apex in a hypertensive child

Table 1
Demographic and clinical data on normotensive and hypertensive children

Variables	Normotensive	Hypertensive	P value
n	34	46	
Age, years	13.1 (3.4)	12.8 (2.6)	0.457
Male Gender, n (%)	22 (65)	33 (72)	0.502
Height, cm	158.4 (16.4)	161.2 (15.8)	0.521
Weight, kg	60.2 (19.3)	69.3 (23.3)	0.065
Body Mass Index	23.4 (4.8)	26.1 (6.5)	0.080
Body mass index percentile, %	75 (26)	82 (23)	0.091
Casual SBP, mmHg	115 (9)	136 (9)	<0.0001
Casual DBP, mmHg	72 (7)	79 (12)	0.0011
Pulse pressure, mmHg	44 (11)	56 (14)	0.0002
Heart Rate, bpm	71 (14)	78 (12)	0.0826
ABPM SBP mean, mmHg	114 (12)	126 (9)	<0.0001
ABPM DBP mean, mmHg	65 (6)	70 (7)	0.0003
ABPM SBP load, %	19 (22)	49 (22)	<0.0001
ABPM DBP load, %	(11)	26 (19)	<0.0001

Variables are written as mean ($\pm$ 1 standard deviation) or percentage. ABPM, ambulatory BP measurement; SBP, systolic BP; DBP, diastolic BP

Table 2
Echocardiographic systolic and diastolic parameters in normotensive and hypertensive children

Variables	Normotensive	Hypertensive	P value
n	34	46	
Relative wall thickness	0.36 (0.07)	0.40 (0.07)	0.012
LVMI, g/m ^{2.7}	37.7 (9.1)	42.62 (10.3)	0.046
Fractional shortening, %	38.6 (6.5)	40.8 (5.6)	0.06
Ejection fraction, %	68.4 (7.5)	71.2 (6.6)	0.073
Mid wall shortening fraction, %	18.5 (3.3)	17.9 (2.5)	0.302
Mitral valve E, cm/s	87.4 (15.9)	94.7 (21.6)	0.072
Mitral valve A, cm/s	44.8 (8.7)	45.5 (14.6)	0.938
Mitral valve E/A	2.0 (0.6)	2.2 (0.7)	0.131
Mitral valve deceleration time, ms	167.1 (40)	168.2 (39)	0.408
Ea (anterior), cm/s	18.4 (4.4)	16.2 (3.9)	0.025
Ea (posterior), cm/s	20.9 (5)	18.7 (3.4)	0.035
Ea (inferior), cm/s	17.2 (3.9)	16.5 (3)	0.552
Ea (septal), cm/s	13.7 (3)	13.3 (2)	0.812
Ea (lateral), cm/s	20.8 (3.9)	19.7 (4.5)	0.121
Ea (radial), cm/s	9.7 (2.5)	11.8 (16.0)	0.673
Aa (anterior), cm/s	8.6 (2.4)	7.7 (2.1)	0.041
Aa (posterior), cm/s	8 (2.3)	7 (1.5)	0.043
Aa (inferior), cm/s	8 (2)	7.6 (2)	0.456
Aa (septal), cm/s	6.9 (1.4)	6.5 (1.5)	0.243
Aa (lateral), cm/s	7.4 (1.8)	7.5 (3.2)	0.366
Aa (radial), cm/s	4.4 (1.8)	5.1 (4.9)	0.452
Ea (average lateral, septal, inferior, posterior, anterior), cm/s	18.1 (3.2)	16.9 (2.6)	0.074
Aa (average lateral, septal, inferior, posterior, anterior), cm/s	7.8 (1.5)	7.22 (1.5)	0.070
Ea/Aa (average lateral, septal, inferior, posterior, anterior), cm/s	2.4 (0.5)	2.4 (0.7)	0.800
E/ Ea (septal), cm/s	6.6 (1.4)	7.2 (1.8)	0.070
E/ Ea (lateral), cm/s	4.3 (0.9)	5.0 (1.2)	0.003
E/ Ea (average septal and lateral), cm/s	2.6 (0.5)	2.9 (0.7)	0.009
Vp, cm/s	62.6 (10.9)	67.1 (15.1)	0.293
E/Vp	1.4 (0.3)	1.44 (0.3)	0.502

Variables are written as mean ($\pm$ 1 standard deviation) ; LVMI left ventricular mass index. E and A, transmitral Doppler E and A wave velocities respectively; Vp, Velocity of propagation (n=67). Tissue Doppler measurements: Ea (anterior) (n=78), Ea (posterior) (n=77), Aa (anterior) (n=78), Aa (posterior) (n=77), E/ Ea (lateral) (n=79),

Table 3
Laboratory values in normotensive and hypertensive children

Variables	Normotensive	Hypertensive	p value
n	34	46	
Serum creatinine, mg/dL	0.71 (0.194)	0.69 (0.18)	0.782
Total cholesterol, mg/dL	159.5 (27.6)	172 (35.3)	0.106
Triglycerides, mg/dL	73.4 (33.4)	83.8 (50.9)	0.667
High Density Lipoprotein, mg/dL	48.8 (9.34)	44.9 (12.4)	0.933
Low Density Lipoprotein, mg/dL	101.6 (28.5)	107.9 (31.3)	0.338
Fasting glucose, mg/dL	63.1 (14.6)	66.3 (13.6)	0.468
Fasting insulin, IU	8.4 (3.9)	13 (10.8)	0.190
QUICKI	0.3 (0.07)	0.3 (0.08)	0.172

Variables are written as mean ($\pm$ 1 standard deviation) or number; QUICKI, Quantitative Insulin Sensitivity Check Index. Triglycerides (n=79), HDL (n=73), LDL (n=71), Fasting insulin (n=74), QUICKI (n=74)

Table 4

Multivariate Linear Regression Models

	Ea (anterior), cm/s		Ea (posterior), cm/s		Aa (anterior), cm/s		Aa (posterior), cm/s		E/ Ea (lateral), cm/s		E/ Ea (average septal and lateral), cm/s	
	Coefficient ± SE	p- value	Coefficient ± SE	p- value	Coefficient ± SE	p- value	Coefficient ± SE	p- value	Coefficient ± SE	p- value	Coefficient ± SE	p- value
<u>Hypertension</u>	-1.8±1.1	.096	-2.2 ±	.049	-1.4 ± .6	.027	-1.1 ± .5	.026	.4 ± .3	.206	.2 ± .2	.334
<u>Age, years</u>	.4 ± .2	.050	.1 ± .2	.493	.05 ± .1	.600	-.01 ± .1	.863	-.1 ± .05	.110	-.05 ± .02	.060
<u>Male Gender</u>	-1.4 ± 1.1	.202	-.4 ± 1.2	.748	.2 ± .1	.707	.4 ± .5	.426	.5 ± .3	.140	.3 ± .2	.104
<u>BMI Percentile</u>	.02 ± .02	.365	.05 ± .02	.040	0 ± .01	.756	.01 ± .01	.247	-.01 ± .01	.205	0 ± 0	.312
<u>AA Race</u>	-1.1 ± 1.4	.433	.01 ± 1.4	.993	.8 ± .8	.313	.4 ± .6	.524	.5 ± .4	.186	.2 ± .2	.323
<u>Hispanic Race</u>	-1.5 ± 1.2	.186	-1.1 ± 1.2	.350	.4 ± .7	.570	1.7 ± .5002	.002	.6 ± .3	.079	.2 ± .2	.312
<u>LVH</u>	-1.3 ± 1.0	.226	.4 ± 1.1	.696	-.8 ± .6	.188	-.8 ± .5	.086	-.2 ± .3	.389	-.1 ± .2	.585
<u>Total Cholesterol, mg/dL</u>	-.02 ± .1	.302	-.002 ± .02	.906	0 ± .009	.361	0 ± .01	.996	0 ± 0	.733	0 ± 0	.712
<u>Fasting Insulin, IU</u>	.02 ± .06	.714	-.08 ± .07	.209	.07 ± .04	.058	0 ± .03	.957	.04 ± .02	.021	.02 ± .01	.014

Linear regression analysis controlling for demographic covariates, LVH, and non-collinear laboratory values. BMI, body mass index; A-A, African American; LVH, left ventricular hypertrophy