

Research Article

Detection of early diastolic alterations by Tissue Doppler Imaging in untreated childhood-onset essential hypertension

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Abstract

The 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). 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. 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 that had a statistically significant change compared with the control children, were regional mitral Ea, Aa, and the E/Ea ratio by TDI. In comparison with 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. 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. *J Am Soc Hypertens* 2014;8(5):303–311. © 2014 American Society of Hypertension. All rights reserved.

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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 of which are 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 diabetes¹⁵ 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 volume¹⁴ 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 (ABPM).

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 BP¹⁷ value specific for their gender, age, and height-percentile underwent a second set of BP measurements 1 to 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 to 2 weeks later. Students with elevated BP on all three 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 three 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 two 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

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