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Left Ventricular Diastolic Dysfunction Assessed by Conventional Echocardiography and Spectral Tissue Doppler Imaging in Adolescents With Arterial Hypertension

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Abstract: Compared to conventional echocardiography, spectral tissue Doppler imaging (s-TDI) allows more precise evaluation of diastolic cardiac function. The purpose of this study was to conduct s-TDI to analyze the slow movement of the left ventricular (LV) myocardium in adolescents with systemic arterial hypertension (HT) and to determine whether patients with HT suffer from LV diastolic dysfunction. The study group comprised 69 consecutive patients (48 boys and 21 girls aged 14–17 years [mean, 15.5 ± 1.1 years]) with primary HT, and the control group comprised 48 healthy participants (24 boys and 24 girls aged 14–17 years [mean, 15.8 ± 1.3 years]). Physical examinations, 24-hour arterial blood pressure monitoring, conventional 2-dimensional and Doppler echocardiography, and s-TDIs were performed. Analysis revealed that study group participants were significantly heavier and had greater LV mass indices than controls ($P < 0.001$). There were no differences between the velocities of E waves (peak early filling of mitral inflow), but the deceleration times of the mitral E waves were significantly shorter whereas the A waves survived longer in the study group than in the control group. The velocities of A waves (peak late filling of mitral inflow) were elevated ($P = 0.041$), and the E/A wave pattern ($E/A = 1.8 \pm 0.4$) was normal. These results suggest pseudonormalization, a type of LV diastolic dysfunction in adolescents with HT.

In the study group, when the sample volume was positioned at the septal or lateral insertion site of the mitral leaflet, the e' wave velocity was significantly depressed whereas the a' wave velocity was elevated, compared to those of the control group ($P < 0.001$).

Editor: Roman Leischik.

Received: November 23, 2014; revised: January 20, 2016; accepted: January 22, 2016.

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Publication was supported by the Faculty of Medicine of Jagiellonian University Medical College (Leading National Research Centre 2012–2017).

The authors have no funding and conflicts of interest to disclose.

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ISSN: 0025-7974

DOI: 10.1097/MD.0000000000002820

The e'/a' ratios from the septal and lateral insertion sites were lower, whereas the E/e' ratio from the septal insertion site was significantly higher in the study group, similar to that seen in atrial reversal velocity ($P < 0.001$).

These findings indicate that using sTDI to find and measure diastolic LV failure is valuable when the probe is placed at the septal and lateral mitral valve annuli during examination.

Changes in the myocardium appear similar to those seen in adults.

(*Medicine* 95(8):e2820)

Abbreviations: 2DE = 2-dimensional echocardiography, A = wave of late filling, BMI = body mass index, BP = blood pressure, BSA = body surface area, DT = deceleration time, E = wave of early filling, EF = ejection fraction, HT = arterial hypertension, IVRT = isovolumetric relaxation time, LA = left atrium, LV = left ventricle, MV = mitral valve, s-TDI = spectral tissue Doppler imaging, TDI = tissue Doppler imaging.

INTRODUCTION

Arterial hypertension (HT) has increasingly become a health problem for adults and children because it leads to many organ lesions, especially in the cardiovascular system, and it may intensify over time if a patient is not appropriately treated. Regular routine blood pressure measurements allow diagnosis at an early stage.

Blood pressure (BP) measurements, especially in children and adolescents, depend on many determinants, such as age, sex, and body size, as well as technical considerations. Therefore, measurement standards must be respected.^{1–3} Correct cuff size and measurement technique, for example, are fundamental for proper interpretation.⁴

A secondary effect of HT on the heart is concentric hypertrophy of the left ventricle (LV). Another complication is cardiac failure, and this is attended by LV dilatation. Consequently, the elevation of LV diastolic pressure is associated with raised pressure in the left atrium (LA). In adults, it may lead to the development of pulmonary HT and changes in the pulmonary vascular bed.⁵

Patients with HT who have not yet presented left ventricle hypertrophy during resting echocardiography may have heart failure symptoms only during exercise. Most often, this is exertional dyspnea. The cause of myocardial dysfunction in these patients is not clear, but we now take into account the stiffness of the myocardium and cardiac myocardial relaxation.

The gold standard for diagnosing diastolic dysfunction is the set of pressure–volume curves obtained by direct invasive measurement. This allows for the assessment of LV filling pressures, relaxation, and stiffness. From a practical point of view, this is not feasible for routine clinical practice; therefore,

Doppler echocardiography remains the principal clinical tool for assessment of LV diastolic function.

When the LV filling pattern is evaluated by conventional echocardiography, diastolic function can be assessed using the mitral inflow signal, and the presence and severity of diastolic dysfunction can be determined. Specifically, diastolic dysfunction alters the relationship between E wave (early filling) and A wave (late filling) as well as deceleration time (DT) of early filling velocity. The third parameter is the isovolumetric relaxation time (IVRT).

When diastolic dysfunction appears, there are 3 stages^{5,6} Stage I is mild diastolic dysfunction (impaired relaxation) resulting in a compensatory increase in flow velocity from atrial contraction. Consequently, the E wave decreases whereas the IVRT increases, and the DT becomes prolonged. Stage II is moderate diastolic dysfunction (pseudonormal pattern), where LV compliance is reduced, resulting in increased LA pressure to compensate for the impaired LV relaxation, maintaining cardiac output. In this situation, the E wave is taller than the A wave (E/A ratio is normal), whereas the DT and IVRT are decreased. Stage III (restrictive) appears with progression of LV diastolic dysfunction in which a severe decrease in compliance leads to further elevation of LA pressure, a very high E wave, and a low A wave, significantly decreasing DT.

Modern echocardiography is equipped with a spectral tissue Doppler imaging (s-TDI) option that measures slow peak velocities of the myocardial motion. Placing the sample volume directly in the myocardium enables more precise evaluation of myocardial movement dynamics and enables detection of discrete lesions (e.g., LV diastolic dysfunction), which are nearly impossible to detect using classic echocardiography.^{5,7}

This technique is an important and useful tool in assessing especially LV diastolic function in adult patients with artificial valve implants as well as those with HT, myocardial infarction, and many other diseases. The TDI (tissue Doppler imaging) also can be used to assess systolic and diastolic velocities in some congenital heart defects.

Eidem et al⁸ evaluated increased LV afterload in individuals with aortic valve stenosis who presented with significantly decreased early diastolic myocardial velocities. They pointed out that increased chronic LV afterload in children is associated with decreased TDI velocities. Moreover, these patients did not have any other identifiable abnormalities of LV function. Therefore, if using a method other than TDI, the beginnings of subclinical LV dysfunction can accidentally be overlooked.

Khouri and colleagues⁶ note that in the adult population, 40% to 50% of patients with congestive heart defects have maintained LV systolic function. However, diastolic dysfunction, unfortunately, is often not diagnosed clinically and consequently affects mortality. In the elderly, diastolic dysfunction of the LV is common and has a significant impact on the deterioration of systolic function.

These situations are well documented in adults, but there is little literature concerning this problem in adolescents. This is particularly important when confronting the constantly increasing population of adolescents worldwide with obesity and HT.

The purpose of this study was to analyze conventional echocardiographic parameters as well as movement of the LV myocardium using s-TDI in adolescents with HT and to determine whether they suffer from insufficient LV function (mainly diastolic) in a way similar to that seen in adults.

METHODS

Patient Population

This cross-sectional study was performed at the Silesian Child Health Center in Katowice (Poland) and included 69 consecutive patients (48 boys and 21 girls) aged 14 to 17 years (mean, 15.5 ± 1.1 years) with primary HT and normal ejection fractions (EFs). The patients had no cardiovascular risk factors, with the exception of obesity, which might influence the etiology of HT. No patient had aortic coarctation or other cardiological or endocrinological problems that could significantly increase afterload and induce LV dysfunction.

The control group consisted of 48 normotensive participants (24 boys and 24 girls) aged 14 to 17 years (mean 15.8 ± 1.3 years) who presented no congenital or acquired heart disease and who were observed for other reasons irrelevant to heart function and heart hypertrophy in echocardiography. Thirty patients (62.5%) suffered from syncope and 18 (37.5%) had nonspecific chest pain.

Efforts were made to match our hypertensive patients to controls. In the first step, age, sex, body mass index (BMI), body mass area, EF (estimated in 2-dimensional echocardiography by the Simpson method), and LV mass index were calculated for all participants.

Inclusion and Exclusion Criteria

We included patients diagnosed with primary HT, observed for at least 3 months, who had not been treated pharmacologically and whose systolic arterial BP levels exceeded 50% of normal, measured using 24-hour continuous monitoring.

We excluded patients with secondary HT, "white coat" arterial HT, or hypertrophy of the myocardium caused by diseases other than HT, patients treated with steroids or cardiodepressants, patients diagnosed with endocrinological or metabolic disorders, and patients with rates of abnormal results lower than 50% during 24-hour BP monitoring.

Measurements

Physical examination included estimation of peripheral pulse characteristics. In addition, a 3-fold arterial BP measurement was conducted using the Korotkoff method. Arterial BP was then continuously monitored for 24 hours using the Reynolds Tracker NIBP ABPM Blood Pressure Recorder in each patient from the study group as well as the control group. Blood pressure measurements were performed in accordance with the American Heart Association standards.⁴ Patients were imaged using a Philips 7500 ultrasound machine with a 3 to 7 MHz wave frequency sector array equipped with an s-TDI option.

We performed conventional 2-dimensional echocardiography measurements including LV mass index, EF, and conventional pulsed-wave and continuous wave Doppler indices according to a consensus document for diastolic function evaluation.^{5,6,9}

We then assessed the e' waves (passive LV filling, early diastolic) and a' waves (atrial contraction, late diastolic) when the sample volume was placed in the apical view at the septal mitral valve (MV) annulus (parabasal segment of the interventricular septum) and the lateral MV annulus (parabasal segment of the LV posterior wall).

The E/ e' ratio, transmitral inflow velocities, E wave DT of early filling velocity, pulmonary vein flow (peak systolic [S velocity] and peak antegrade diastolic [D velocity]), as well as atrial reversal (Ar) velocity and A wave duration (obtained at the

level of the mitral annulus) were also measured. The EF and LV mass indices were calculated to determine whether differences between the groups were caused by modifications in LV geometry, mass, or function.

Statistical Analysis

Statistica 10 software was used for calculations. To evaluate the differences between the experimental and control groups, Student’s *t* test was used. The values subject to comparison were significantly different when *P* < 0.05. Before analyzing the differences, distributions of the variables were verified. After performing further tests (i.e., the Kolmogorov–Smirnov test with the Lilliefors amendment and the Shapiro–Wilk test as well as the central limit theorem), we found that the distributions of the measured variables did not depart significantly from the normal distribution. Discriminant function analysis was also performed, and the obtained matrix showed the structure of the variables that were the most and least different in the study and control groups.

The research protocol was approved by the Bioethical Commission of Medical University of Silesia (No. NN-6501-174/07) and, therefore, was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

RESULTS

We first determined the normal values for adolescents aged 14 to 17 years. Our control group (*N* = 48) was younger than those analyzed by Nagueh et al⁵ (aged 16–20 years, 21–40 years, 41–60 years, and 60 years or older). However, our results closely correspond with the normal values and trends seen among Doppler-derived diastolic measurements (Table 1).

In total, 30 parameters were evaluated in detail and analyzed statistically. Three (i.e., age, BMI, body surface area [BSA]) were general parameters whereas 27 concerned echocardiography; 8 parameters were measured using s-TDI (Tables 2 and 3).

The patients from the research group were properly selected and matched by age (*P* = 0.14), although the BMIs, BSAs, and LV masses were significantly higher in the study group (*P* < 0.001 [Table 2]).

The study group demonstrated 75.63% (range 51–98.5%) elevated BP during the day and night, on average, compared to those in the control group (data not shown).

Statistical analysis showed no difference in IVRT and E-MV (peak early diastolic transmitral flow velocities) between the study and control groups (*P* > 0.05). However, the A-MV (peak late diastolic transmitral flow velocities) were higher in the study group than in the control group, resulting in lower E/A ratios (*P* < 0.001). Also, the DTs and septal and lateral *e'* waves were lower. Similarly the *e'/a'* ratio from the septal and lateral insertion sites of the mitral leaflets was lower in the study group (*P* < 0.001).

On the contrary, *a'* waves from the same segments (septal and lateral) were significantly higher (*P* < 0.001 and *P* = 0.013, respectively). Septal E/*e'* ratios and pulmonary venous Ar velocity waves were also significantly higher in the study group (*P* < 0.001), whereas the S waves in the systolic pulmonary venous flow were lower, as were PV S/D ratios of peak systolic and peak diastolic pulmonary venous flow (*P* < 0.001 [Tables 3 and 4]).

In summary, we found that in adolescents with HT, the values for IVRT, E-MV, PV-D (peak anterograde diastolic

velocity), and E/*e'* ratio using lateral insertion do not change. However, significantly higher values were recorded for the speed of the A-MV wave at the time of inflow through the mitral valve as well as the speed of myocardium movement (wave *a'*). Also, the E/*e'* ratio was elevated. In contrast, significantly decreased values were presented for *e'* waves derived from the septal and lateral segments, whereas E/A ratios and DTs were depressed (Table 4). This might suggest the beginning of pseudonormalization, a type of LV diastolic failure.

Analysis of the structure matrix showed that the strongest features differentiating the groups were septal *e'/a'* ratio, septal *e'* and *a'*, LV mass index, Ar, and DT, whereas the weakest were lateral *e'* and *a'*, A-MV, IVRT, EF, and E-MV (data not shown).

DISCUSSION

Systemic HT is one of the most important factors in the appearance of complications in the cardiovascular system. This issue is particularly important in children and adolescents with obesity, where prevention is sometimes implemented too late.^{10,11}

The prevalence of primary HT in adolescents is low; it is more common to see the secondary type. The usual causes of secondary HT in this age group are renal diseases and coarctation of the aorta. In recent years, among teenagers aged 14 to 18 years, there has been an increase in drug use, particularly anabolic energizing preparations. These substances can lead to increased BP and secondary organ damage.^{12–14}

Body weight, lipid metabolism disorders, improper lifestyle, and diet play important roles in the etiology of HT.^{10,15} In adults, one of the secondary complications of HT is cardiac hypertrophy, which can also be detected in the adolescent

TABLE 1. Normal Values for Doppler-Derived Diastolic Measurements for Adolescents Aged 14 to 17 years (Data Completed per the Recommendations for Evaluation of Left Ventricular Diastolic Function by Echocardiography (Nagueh et al)⁵

Age Group 14–17 (y)	Mean	Min–Max
IVRT (ms)	67 ± 8	(50–90)
E/A ratio	2.1 ± 0.4	(1.3–3.1)
DT (ms)	157.8 ± 29.9	(119–260)
A dur (ms)	103.2 ± 14.6	(84.3–165)
PV S/D ratio	1.1 ± 0.1	(0.9–1.4)
PV Ar (cm/s)	18.6 ± 4.1	(11–30)
PV Ar duration (ms)*		
Septal <i>e'</i> (cm/s)	16.3 ± 1.7	(13.8–21.7)
Septal <i>e'/a'</i> ratio	3.2 ± 0.7	(2.0–5.1)
Lateral <i>e'</i> (cm/s)	18.8 ± 2.7	(13.4–25)
Lateral <i>e'/a'</i> ratio	3.4 ± 0.9	(1.9–5.6)

* No data. IVRT = isovolumetric relaxation time, E/A ratio = mitral E wave velocity/mitral A wave velocity, E-MV = peak early diastolic transmitral flow velocity, DT = deceleration time, A dur = mitral A-wave duration, PV S/D ratio = peak systolic pulmonary venous flow/peak anterograde diastolic pulmonary velocity, PV Ar = peak atrial reversal velocity, PV Ar dur = pulmonary venous Ar duration, Septal *e'* = wave of early diastolic septal mitral valve annular velocity, Septal *a'* = wave of late diastolic septal mitral valve annular velocity, Lateral *e'* = wave of early diastolic lateral mitral valve annular velocity, Lateral *a'* = wave of late diastolic lateral mitral valve annular velocity.

TABLE 2. Clinical and Conventional Echocardiographic Parameters

	Group											
	Study (N = 69)					Control (N = 48)					Test Statistics	
	M	SD	Me	MIN	MAX	M	SD	Me	MIN	MAX	tStudent	P
No significant differences between the study group vs control												
Age (y)	15.5	1.1	16.0	14.0	17.0	15.8	1.3	16.0	14.0	18.0	-1.462	0.14
LVIDD (mm)	46.5	6.0	45.8	32.2	59.9	45.0	5.0	44.1	35.4	56.7	1.201	0.23
LVIDS (mm)	28.2	5.0	27.7	12.3	37.3	28.0	3.0	27.4	21.4	35.0	0.266	0.74
EF (2DE) (%)	68.9	4.9	69.0	61.0	79.0	67.7	3.9	68.0	61.0	77.0	1.434	0.15
Significantly ELEVATED values in the study group vs control												
BMI	25.5	4.1	24.8	18.4	36.2	21.5	3.7	21.2	15.7	36.8	5,390	<0.001
BSA (sqm)	1.9	0.3	1.9	1.4	2.6	1.7	0.2	1.6	1.4	2.1	4,496	<0.001
LV mass dI (g/m ²)	68.9	17.1	66.1	37.4	103.0	54.8	11.5	54.5	37.0	83.6	4,969	<0.001
LV mass sI (g/m ²)	72.9	17.2	73.1	39.0	107.0	52.7	11.1	51.0	31.9	78.1	7,144	<0.001
IVSD (mm)	9.3	2.5	9.0	5.1	17.0	6.6	0.1	6.4	4.6	9.2	5,672	<0.001
IVSS (mm)	13.9	2.8	13.8	8.7	23.3	9.2	1.4	9.2	6.8	13.1	8,612	<0.001
LVPWD (mm)	8.2	1.9	7.8	4.7	15.3	6.3	0.12	6.1	4.5	10.4	5,117	<0.001
LVPWS (mm)	16.1	3.0	15.8	11.0	23.4	11.9	1.9	11.9	7.2	15.8	6,828	<0.001

BMI = body mass index, BSA = body surface area, EF = ejection fraction, IVSD = interventricular septum in diastole, IVSS = interventricular septum in systole, LV mass dI = indexed left ventricular mass in diastole, LV mass sI = indexed left ventricular mass in systole, LVIDD = left ventricular internal diameter in diastole, LVIDS = left ventricular internal diameter in systole, LVPWD = left ventricular posterior wall diameter in diastole, LVPWS = left ventricular posterior wall diameter in systole, M = average, MAX = maximum, Me = mediana, MIN = minimum, P = P value the difference is significant at P value < 05, SD = standard deviation.

TABLE 3. Parameters Obtained in Conventional Echocardiography and Spectral Tissue Doppler Imaging

	Group											
	Study (N = 69)					Control (N = 48)					Test Statistics	
	M	SD	Me	MIN	MAX	M	SD	Me	MIN	MAX	Student's t	P
conventional Doppler echocardiography												
IVRT (ms)	71.0	1.2	70.0	50.0	100.0	67.0	8.0	70.0	50.0	90.0	1.732	0.086
E-MV (cm/s)	85.7	17.1	85.8	51.7	145.0	89.9	15.6	87.9	65.0	131.0	-1.340	0.183
A-MV (cm/s)	48.8	13.8	47.0	23.8	99.9	44.1	9.3	42.0	31.8	79.8	2.068	0.041
E/A	1.8	0.4	1.8	1.0	3.4	2.1	0.4	2.0	1.3	3.1	-3.686	<0.001
DT (ms)	127.3	17.4	130.0	84.0	195.0	157.8	29.9	149.3	119.0	260.0	-6.965	<0.001
A dur (ms)	119.0	13.8	119.0	96.0	165.0	103.2	14.6	99.7	84.3	165.0	5.948	<0.001
PV S (cm/s)	52.5	9.2	53.0	31.0	69.0	58.7	8.6	58.0	41.7	78.0	-3.712	<0.001
PV D (cm/s)	54.1	7.6	54.0	37.0	69.0	52.9	8.5	53.5	39.5	69.0	0.787	0.433
PV S/D	1.0	0.2	1.0	0.1	1.3	1.1	0.1	1.1	0.9	1.4	-5.693	<0.001
Ar (cm/s)	25.1	5.4	24.0	15.0	36.0	18.6	4.1	19.0	11.0	30.0	7.057	<0.001
spectral tissue Doppler imaging												
Septal e' (cm/s)	12.9	1.8	13.2	9.3	17.0	16.3	1.7	16.2	13.8	21.7	-10.160	<0.001
Septal a' (cm/s)	7.0	1.3	6.8	4.1	10.5	5.2	1.0	5.2	3.2	7.4	7.907	<0.001
Septal e'/a'	1.9	0.4	1.9	1.1	3.5	3.2	0.7	3.2	2.0	5.1	-13.046	<0.001
E/e' septal	6.7	1.7	6.5	3.1	13.8	5.5	1.1	5.2	3.8	8.8	4.172	<0.001
Lateral e' (cm/s)	17.3	3.1	17.2	10.4	25.3	18.8	2.7	19.0	13.4	25.0	-2.717	0.008
Lateral a' (cm/s)	6.6	1.8	6.7	3.1	11.9	5.9	1.3	5.7	3.4	9.1	2.510	0.013
Latetal e'/a'	2.8	0.9	2.8	1.4	5.0	3.4	0.9	3.1	1.9	5.6	-3.753	<0.001
E/e' Lateral	5.1	1.4	4.9	3.4	7.6	4.9	1.0	4.8	3.3	7.6	0.901	0.36

A dur = mitral A-wave duration, A-MV = peak late diastolic transmitral flow velocity, Ar = atrial reversal velocity, DT = deceleration time, E/A = ratio E wave to A wave, e'/a' = ratio e' wave to a' wave, E-MV = peak early diastolic transmitral flow velocity, IVRT = isovolumetric relaxation time, Lateral a' = wave of late diastolic lateral mitral valve annular velocity, Lateral e' = wave of early diastolic lateral mitral valve annular velocity, M = average, MAX = maximum, Me = mediana, MIN = minimum, P = P value the difference is significant at P value < .05, PV D = peak anterograde diastolic pulmonary velocity, PV S/D = ratio S wave to D wave, PV S = peak systolic pulmonary venous flow, SD = standard deviation, Septal a' = wave of late diastolic septal mitral valve annular velocity, Septal e' = wave of early diastolic septal mitral valve annular velocity.

TABLE 4. Results of Statistical Analyses of Normal, Significantly Elevated, and Significantly Depressed Values in the Study and Control Groups

	Group										Test Statistics	
	Study (N = 69)					Control (N = 48)					Student's <i>t</i>	<i>P</i>
	M	SD	Me	MIN	MAX	M	SD	Me	MIN	MAX		
No significant differences between the study group vs control												
IVRT (ms)	71.0	1.2	70.0	50.0	100.0	67.0	8.0	70.0	50.0	90.0	1.732	0.086
E-MV (cm/s)	85.7	17.1	85.8	51.7	145.0	89.9	15.6	87.9	65.0	131.0	-1.340	0.183
PV D (cm/s)	54.1	7.6	54.0	37.0	69.0	52.9	8.5	53.5	39.5	69.0	0.787	0.433
E/e' lateral	5.1	1.4	4.9	3.4	7.6	4.9	1.0	4.8	3.3	7.6	0.901	0.36
Significantly ELEVATED values in the study group vs control												
A-MV (cm/s)	48.8	13.8	47.0	23.8	99.9	44.1	9.3	42.0	31.8	79.8	2.068	0.041
Septal a' (cm/s)	7.0	1.3	6.8	4.1	10.5	5.2	1.0	5.2	3.2	7.4	7.907	<0.001
Lateral a' (cm/s)	6.6	1.8	6.7	3.1	11.9	5.9	1.3	5.7	3.4	9.1	2.510	0.013
E/e' Septal	6.7	1.7	6.5	3.1	13.8	5.5	1.1	5.2	3.8	8.8	4.172	<0.001
A dur (ms)	119.0	13.8	119.0	96.0	165.0	103.2	14.6	99.7	84.3	165.0	5.948	<0.001
Ar (cm/s)	25.1	5.4	24.0	15.0	36.0	18.6	4.1	19.0	11.0	30.0	7.057	<0.001
Significantly DEPRESSED values in the study group vs. control												
E/A	1.8	0.4	1.8	1.0	3.4	2.1	0.4	2.0	1.3	3.1	-3.686	<0.001
DT (ms)	127.3	17.4	130.0	84.0	195.0	157.8	29.9	149.3	119.0	260.0	-6.965	<0.001
Septal e' (cm/s)	12.9	1.8	13.2	9.3	17.0	16.3	1.7	16.2	13.8	21.7	-10.160	<0.001
Lateral e' (cm/s)	17.3	3.1	17.2	10.4	25.3	18.8	2.7	19.0	13.4	25.0	-2.717	0.008
Septal e'/a'	1.9	0.4	1.9	1.1	3.5	3.2	0.7	3.2	2.0	5.1	-13.046	<0.001
Latetal e'/a'	2.8	0.9	2.8	1.4	5.0	3.4	0.9	3.1	1.9	5.6	-3.753	<0.001
PV S (cm/s)	52.5	9.2	53.0	31.0	69.0	58.7	8.6	58.0	41.7	78.0	-3.712	<0.001
PV S/D	1.0	0.2	1.0	0.1	1.3	1.1	0.1	1.1	0.9	1.4	-5.693	<0.001

A dur = mitral A-wave duration, A-MV = peak late diastolic transmitral flow velocity, Ar = atrial reversal velocity, DT = deceleration time, E/A = ratio E wave to A wave, E/e' = ratio E wave to e' wave, e'/a' = ratio e' wave to a' wave, E-MV = peak early diastolic transmitral flow velocity, IVRT = isovolumetric relaxation time, Lateral a' = wave of late diastolic lateral mitral valve annular velocity, Lateral e' = wave of early diastolic lateral mitral valve annular velocity, M = average, MAX = maximum, Me = mediana, MIN = minimum, P = P value the difference is significant at P value < 0.05, PV D = peak anterograde diastolic pulmonary velocity, PV S/D = ratio S wave to D wave, PV S = peak systolic pulmonary venous flow, SD = standard deviation, Septal a' = wave of late diastolic septal mitral valve annular velocity, Septal e' = wave of early diastolic septal mitral valve annular velocity.

population, although organ changes are more discrete than in adults.⁵ Cardiac hypertrophy, mainly hypertrophy of the septum and posterior wall of the LV as well as enlargement in the diastole, is believed to also be present in adolescents with HT.¹⁶ Chronic HT results in remodeling in the myocardium as well as changes in the blood vessels and organs (peripheral arteries, retina, kidney, and brain).

The Framingham Heart Study¹⁷ showed that an increase in LV mass predicts a higher incidence of clinical events, including death, attributable to cardiovascular disease. Mu et al¹⁸ indicated that ultrasound speckle tracking imaging may be helpful for the detection of early changes in LV diastolic function in hypertensive patients.

Palmiero et al,¹⁹ in a recent publication (2015), emphasized that "evaluation of left ventricular diastolic function should be an integral part of routine examination of hypertensive patients, and that Doppler echocardiography is the best toll for early detection of left ventricle diastolic dysfunction."

In conventional Doppler echocardiography, prolonged IVRT can indicate developing diastolic heart failure; however, it has several limitations and is not currently sensitive enough for detecting diastolic heart failure. Indeed, we found that the IVRT did not differ between study and control groups (P > 0.05). But, its prolongation usually precedes the

appearance of LV hypertrophy.²⁰ When early LV filling was decreased, as expressed through reduction in E wave amplitude, the E/A wave ratio was also reduced.

Our study involved adolescents with primary HT and normal LV EFs (68.9% ± 4.9%), although they suffered from the LV hypertrophy that reduced compliance.

Nagueh et al⁵ reported that in healthy individuals aged 16 to 20 years, the E/A ratio is 1.88 ± 0.45. In our study group, aged 14 to 17 years, the ratio was almost identical (1.8 ± 0.4), but it was lower than that seen in the control group (2.1 ± 0.4 [P < 0.001]). Therefore, because the E/A pattern was normal whereas DT was evidently decreased, this can indicate that our study group may present 2nd stage LV diastolic failure (pseudonormal LV filling).

The TDI method enables direct assessment of myocardial function by measuring LV velocity during systole and diastole. The RICH-Q study documented that TDI is a valuable method for assessing segmental function of the myocardial wall in children and adolescents with renal disease.²¹

The specific movement of myocardial segments in s-TDI is characterized by 3 basic swings. One is the s wave, corresponding to systolic muscle movement and comprising 2 components, the s1 wave (the early period of contraction) and the s2 wave (the period of late systole). A second is the e' wave,

corresponding to diastolic movement during rapid ventricular filling. Third is the a' wave, corresponding to diastolic motion during atrial contraction. In the assessment of segmental LV systolic and diastolic function, visualization of the maximum deflection of s' , e' , and a' waves is particularly useful. Wilkenshoff et al²² established standards for assessment; however, these standards are for people aged 20 to 69 years.

In adult patients with HT, the s-TDI method revealed reduced velocity in the e' waves and a reduced e'/a' wave ratio, indicating advanced diastolic dysfunction.²³ We found a similar result, and the e'/a' ratio was significantly reduced in the study group, compared to controls. An ASCOT substudy revealed that TDI is an effective tool for assessing cardiac risk in a hypertensive population. The sample volume showed slower velocities when placed at the septal MV annulus than when placed at the lateral annulus.²⁴ Our study revealed similar findings.

Dalen and colleagues²⁵ presented an analysis of cardiovascular risk factors (i.e., BP, BMI, serum lipids, glucose, and renal function) in a low-risk population and correlated these factors with systolic and diastolic cardiac function. They suggested that conventional risk factors predict cardiac function many years before the onset of clinical disease. Cantinotti and Lopez²⁶ noted that interest in estimating diastolic function in children has recently increased, but emphasized that pediatric diastolic nomograms in TDI in neonates and children are limited by small sample sizes and inconsistent methodologies for the performance and normalization of measurements. To date, standards for the pediatric population have not been definitively established.

In this work, s-TDI was used to assess changes in the LV myocardium in adolescents with HT. Use of this method in such a group has not been widely described in the literature. Based on our research, we found that the e' waves in the septal as well as the lateral insertion sites of the mitral leaflets and the a' waves from the same locations were significantly different and reversed in adolescents with HT than in our control group. The e' wave values were significantly lower, whereas the a' wave values were higher than those in the healthy sample.

This finding has important value because in conventional Doppler echocardiography, flows through the mitral valve and function of the left ventricle were normal, erroneously suggesting normal LV function.

Additionally, the results obtained from s-TDI (i.e., a decrease in the e' wave, increase in the a' wave, and increase in E/e' ratio) support the observation that our patients have developed LV diastolic failure.

Gaasch and Little,²⁷ in an editorial article, present a very interesting discussion and explain the relationship between the E and e' waves and the importance of these values in diastolic heart failure. They conclude that an increase in the E/e' ratio indicates elevated left atrial pressure and provides an echocardiographic indication of LV diastolic insufficiency.

Meanwhile, Fici et al²⁸ revealed that diastolic dysfunction is frequently detected in the earlier uncomplicated phases of the disease and that s-TDI may detect an initial impairment of LV relaxation in patients in whom echo Doppler remains normal. In this context, our findings are consistent with other studies.

This study has some limitations. First, s-TDI measurements have many pitfalls (a small movement in the lateral wall above the annulus leads to varied measurements); therefore, additional measurements are recommended. Second, the global

left atrial strain, useful in estimating left atrial function, was not revealed in this study.^{29–31} Although Leischik et al³² indicates that using strain and strain-rate imaging to assess the LA function were validated, this technique is not currently used in routine clinical practice, and further research is needed to develop clear standards. Third, we did not follow the patients enrolled in this study to evaluate whether regression of diastolic dysfunction was observed during treatment.

However, there are few scientific reports covering the correlation between primary HT and diastolic LV failure in patients from such a young age group.

CONCLUSIONS

Our findings suggest that adolescents with systemic arterial HT can present echocardiographic parameters of LV diastolic dysfunction similar to adults. Results indicate that this may be pseudonormalization (stage II). Additionally, a decreased value of the e' wave and an increased value of the a' wave can be noted on s-TDI examination, and this feature is present when the sample volume is placed in the parbasal septal and lateral sites of the mitral leaflets.

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