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Left Ventricular Diastolic Function in Normotensive Adolescents with Different Genetic Risk of Hypertension

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Summary: Abnormalities of the diastolic function of the left ventricle are the first sign of cardiac involvement in arterial hypertension. We have studied the diastolic function in a group of normotensive adolescents with confirmed family history of hypertension. M-mode echocardiography was performed in 86 normotensive males aged 14–19 years: 41 sons of at least one hypertensive parent (SHT) and 45 sons of normotensive parents (SNT). Cross-sectional area of the left ventricle and left ventricular (LV) mass index were significantly greater in the SHT than in the SNT group (10.05 ± 1.84 vs. 8.9 ± 1.56 cm/m^2, $p < 0.01$ and 129.3 ± 29.3 vs. 109.23 ± 25.7 g/m^2, $p < 0.002$, respectively). No significant difference between the two groups was observed in the indices of left ventricular diastolic function, except for mitral valve opening rate (463.51 ± 90.45 in SHT vs. 416.71 ± 78.84 mm/s in SNT; $p < 0.02$). From the analysis of the subgroup of adolescents having left ventricular mass greater than the upper normal value, we observed that they showed mean time of rapid filling significantly longer than SNT: this could represent an early marker of the pathological character of such hypertrophy. Our results suggest that the higher LV mass observed in the SHT is not associated with chamber and myocardial stiffness abnormalities.

Key words: hypertension, diastolic function, echocardiography, genetic risk of hypertension, cardiac hypertrophy

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Introduction

In arterial hypertension (AH), cardiac hypertrophy is associated with abnormalities of the diastolic function of the left ventricle.[1-5] Such abnormalities are often present in the early stage of AH, even before the development of ventricular hypertrophy.[6-8] In a previous study, we observed that normotensive adolescents with hypertensive parents showed left ventricular mass (LVM) significantly greater than controls.[9] We now report data on the diastolic function of the left ventricle in the same population, in order to elucidate the meaning of the morphologic changes which have been found.

Materials and Methods

We studied 86 normotensive males, aged between 14 and 19 years, whose blood pressure (BP) values had been recorded in three different visits performed at monthly intervals. The upper limit of normal BP was considered the 95th percentile of values obtained in the different age classes for 675 adolescents. The average value of three BP recordings taken after 5 min in a sitting position was considered as the basal value.

Of our subjects, 41 had at least one hypertensive parent (SHT), and 45 had two normotensive parents (SNT). Both parents underwent a BP measurement in order to confirm the parental history of AH. A parent was considered hypertensive if on antihypertensive treatment or if a diastolic BP $\geq$ 95 mmHg was recorded at two different visits. A detailed history of each adolescent was taken and a complete physical examination performed, including the measurement of BP and heart rate in sitting position.

Each subject underwent ECG both at rest and at exercise, as well as an M-mode echocardiogram performed according to the European Society of Cardiology and the American Society of Echocardiography recommendations.[10-13] Subjects whose echocardiograms did not allow us to evaluate all the indices of diastolic performance were excluded from the study. All echocardiographic tracings

were read by the same observer, who ignored the parental history for hypertension of the adolescents.

Other methodological details have been reported elsewhere.[14] Three cardiac cycles were averaged to obtain the following parameters of LV morphology and systolic performance, indexed to body surface area when appropriate: thickness of interventricular septum (IVS) and posterior wall (PW); cross-sectional area of the LV (CSA); left ventricular mass (LVM) utilizing the formula of Devereux and Reichek;[15] fractional shortening (FS); and cardiac index (CI).

The following parameters of LV diastolic function have been calculated by a computerized technique:[16,17] mitral valve opening (DE) and closing (EF) velocities; isovolumic relaxation time (IRT: interval between end-systole and mitral valve opening); rapid filling time (RFT) normalized for the total ventricular filling time; average isovolumic (IRR) and rapid (RFR) filling rates and percentual decrements of PW thickness during isovolumic relaxation (PWIR) and during rapid filling (PWRF).

Statistical Analysis

The statistical significance of the differences between mean values has been tested by the Student's *t*-test for unpaired data. Linear regression analysis between morphologic data and data of diastolic function has also been applied.

Results

Mean values of systolic blood pressure (SBP) at rest, diastolic blood pressure (DBP), and heart (HR) at rest and at peak exercise, body surface area (BSA), and Quetelet index were similar in the two groups; SBP at peak exercise was significantly higher in SHT than in SNT subjects (Table I). Indices of systolic function were similar in the two groups (Table II).

Mean thickness of IVS and PW and other indices of hypertrophy were significantly greater in the SHT group,

TABLE I Clinical data for SNT and SHT

	SNT n=45	SHT n=41	p Value
Age (years)	16.53±1.14	16.79±1.21	NS
SBP (mmHg)	121.18±11.71	125.26±8.93	NS
DBP (mmHg)	60.66±11.98	61.45±10.58	NS
HR (beats/min)	78.31±11.96	75.74±12.65	NS
BSA (m^2)	1.79±0.14	1.75±0.13	NS
BMI (kg/m^2)	20.8±2.0	20.2±2.5	NS
SBP PE (mmHg)	190.8±17.2	199.0±19.7	<0.05
DBP PE (mmHg)	83.3±20.7	83.2±16.5	NS
HR PE (beats/min)	169.8±13.0	167.5±15.3	NS

Abbreviations: SNT=sons of normotensive parents; SHT=sons of hypertensive parents; SBP=systolic blood pressure; DBP=diastolic blood pressure; HR=heart rate; BSA=body surface area; BMI=body mass index; PE=peak exercise.
Values are means±1 SD.

TABLE II Echocardiographic indices of left ventricular morphology and systolic function

	SNT n=45	SHT n=41	p Value
IVST (cm/m^2)	0.48±0.08	0.54±0.08	<0.01
PWT (cm/m^2)	0.49±0.08	0.54±0.11	<0.05
CSA (cm/m^2)	8.90±1.56	10.05±1.84	<0.01
LVM (g/m^2)	109.23±25.07	129.30±29.30	<0.002
SF (%)	33.86±5.52	34.76±4.58	NS
EF (%)	62.24±6.30	63.75±5.48	NS
CI ($l/min/m^2$)	2.89±0.58	2.79±0.71	NS

Abbreviations: IVST=interventricular septal thickness; PWT=posterior wall thickness; CSA=cross-sectional area; LVM=left ventricular mass; SF=shortening fraction; EF=ejection fraction; CI=cardiac index; for other abbreviations, see Table I.
Values are means±1 SD.

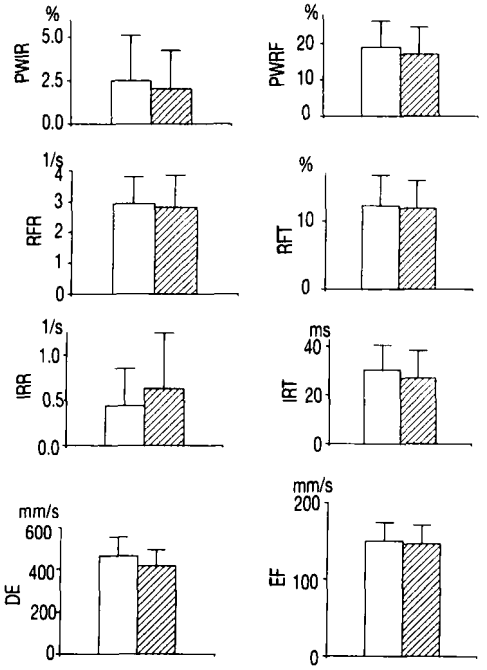

FIG. 1 Indices of left ventricular diastolic function in sons of normotensive parents (□) and in sons of hypertensive parents (▨). PWIR = percentual decrement of posterior wall during isovolumic relaxation; PWRF = percentual decrement of posterior wall during rapid filling; RFR = rapid filling rate; RFT = rapid filling time; IRR = isovolumic relaxation rate; IRT = isovolumic relaxation time; DE = mitral valve opening rate; EF = mitral valve closing rate.

as reported in our previous study (Table II). Mean values of diastolic function indices are reported in Figure 1. EF, IRT, IRR, RFT, and RFR were similar in both groups. Mean values of PWIR and PWRF were greater in SHT than in SNT, but differences did not reach statistical significance; only DE results were significantly higher in SHT than in SNT (463.51 ± 90.45 vs. 416.71 ± 78.84 mm/s; $p < 0.02$).

No correlation between LVM index and diastolic function was observed in our population.

Dividing each group into subsets of adolescents with and without LV hypertrophy (LVM index greater than the upper value of 95% confidence limits in the SNT group), we found 5 subjects with hypertrophy in the SHT group and 1 subject in the SNT group.

In this small group of subjects with SHT with hypertrophy, RFT was significantly greater than in the SNT group (18.81 ± 7.3 vs. $11.73 \pm 3.9\%$; $p < 0.01$), whereas the other diastolic parameters were similar.

Discussion

Some studies have pointed out that the degree of alteration in the pattern of left ventricular filling is directly related to the degree of hypertrophy;[1-5] nevertheless, alterations of the diastolic function, even in absence of hypertrophy, have been detected in mild hypertension.[6-8]

Experimental data[18-20] suggest that moderate and discontinuous stresses acting on the LV wall would result in physiological hypertrophy with normal cardiac function, whereas severe stresses continuously applied would result in a pathological hypertrophy with diastolic function impaired as well. Therefore, it seems that diastolic alterations are determined by the nature of the stress-inducing hypertrophy rather than by hypertrophy itself. In fact, in athletes, a physiological hypertrophy with a normal diastolic function is present,[4,21-26] to a degree similar to that found in such cardiovascular diseases as hypertension and aortic or mitral valvular diseases.[1-5,17,27,28] In our study SHT did not show any impairment of diastolic function, even if LVM was significantly greater than that of SNT. Moreover, a symmetric increase affecting the septum and the posterior wall was found, unlike that observed early in the development of chronic BP overload-related hypertrophy.[29,30] This observation, along with the BP hyperresponsiveness to exercise with normal resting BP values, would support the hypothesis of a similarity between SHT and athletes.

It is known that structural factors, and particularly wall thickness, influence chamber stiffness, whereas myocardial stiffness is related to alterations in the intrinsic elastic properties of the myocardial cell rather than to an increased ventricular mass.[31,32]

Therefore, our findings would suggest that, in SHT, both chamber and myocardial stiffnesses are still physiological in character. Alternatively, we could hypothesize that the observed morphologic changes were not sufficiently extensive to result in alterations of the diastolic function, as the analysis of the subgroup with cardiac hypertrophy could suggest.

In the whole group of SHT adolescents, we observed a significant increase in mitral valve (MV) opening rate and a consensual trend for PWIR and PWRF. This close correlation between LV filling rate and indices of systolic function might be a marker of an augmented sympathetic tone leading to the hyperkinetic state observed by some authors in the early stages of hypertension.[33-36]

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