Myocardial Hypertrophy of the Left Ventricle during Familial Arterial Hypertension

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In patients with familial arterial hypertension and their relatives preclinical signs of myocardial hypertrophy were observed before the formation of stably increased blood pressure. We evaluated echocardiographic sings of left ventricular myocardial hypertrophy in normotensive relatives of patients with arterial hypertension.

Key Words: *left ventricular hypertrophy; arterial hypertension; normotensive relatives*

Pathophysiological mechanisms of hypertrophy of the left ventricle (LV) include the increase in afterload, high blood pressure (BP), high blood viscosity, and increased body weight [2,4,8]. LV hypertrophy is characterized by phenotypical changes in cardiomyocytes that concern contractile and membrane proteins, energy metabolism, electromechanical coupling, endocrine and exocrine functions, cytoskeleton, and extracellular matrix. These changes are accompanied by activation of the renin-angiotensin system in the heart. Published data show that LV hypertrophy can develop in subjects with normal BP [7,9].

Here we studied preclinical signs of LV hypertrophy and diastolic dysfunction during familial essential hypertension (EH).

MATERIALS AND METHODS

We examined 216 patients with familial EH, 132 relative of patients with familial EH, and 130 conventionally healthy volunteers (control group). The degree of LV myocardial hypertrophy and diastolic function of the heart were studied by the method of Doppler echocardiography.

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RESULTS

Signs of LV myocardial hypertrophy and diastolic dysfunction were found in relatives of patients with familial EH. We revealed changes in the maximum rate of early filling (49.8% patients, $p<0.05$), maximum rate of late filling (19.2% patients, $p<0.05$), late filling fraction (33.3% patients, $p<0.05$), and isovolumic relaxation time (8.2% patients, $p<0.05$). In 50% relatives of patients with familial EH one of these indexes of LV filling differed from normal (Table 1).

The index of active relaxation of LV (maximum rate of early filling) in relatives of patients with familial EH was 20.7% below normal. They were characterized by frequent changes in transmitral blood flow, which is typical of LV diastolic dysfunction. Diastolic dysfunction of LV, decreased elasticity of the myocardium, and increase in rigidity of the LV wall due to early myocardial hypertrophy preceded clinical manifestations of EH.

The maximum and normalized rate of early LV filling, stroke volume, cardiac index, and mass index of the LV myocardium were higher in male patients with familial EH.

Echocardiography of the LV myocardium revealed signs of serious diastolic dysfunction in patients with familial EH. Doppler cardiography of diastolic transmitral flow revealed redistribution of

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blood flow to late diastolic filling. The ratio between the maximum rates of early and late filling in LV (E/A) was below 1. These patients had abnormal indexes of LV filling, which reflected diastolic dysfunction: changes in the E/A ratio (86% patients, $p<0.05$), maximum rate of early LV filling (54.4% patients, $p<0.05$), late filling fraction (68.9% patients, $p<0.01$), maximum rate of late filling (63.2% patients, $p<0.05$), isovolumic relaxation time (69.9% patients, $p<0.05$), and early filling deceleration time (16.1% patients, $p<0.05$). In 94% patients with familial EH, at least one index of LV filling differed from normal (Table 2).

A change in transmitral blood flow typical of LV diastolic dysfunction were observed in 80% patients with EH. These changes reflect deceleration of active relaxation (maximum rate of LV early filling, isovolumic relaxation time, and normalized maximum rate of LV early filling), increase in rigidity of the LV wall, and decrease in diastolic function of LV.

The signs of LV diastolic function differed in patients with concentric hypertrophy of LV (maximum rate of early LV filling, E/A, late filling fraction, and isovolumic relaxation time, $p<0.05$). Diastolic dysfunction of LV in patients with familial EH accompanied by concentric remodeling of the heart includes structural changes in the myocardium that develop at the early stage of this disease.

Genetic factors play an important role in the development of cardiovascular disorders. For example, the left ventricular mass index significantly increases in EH patients with the TT genotype of the ATG gene [1,3,5,7]. In animals with spontaneous EH, remodeling of the heart and vessels precedes the development of EH. It was hypothesized that the interaction of genes and neurohormonal, tissue, and circulating myofibril growth factors plays a role in cardiac remodeling during EH. These data provide support for the existence of preclinical EH. Up to 75% individual variations in the weight of the myocardium are determined by genetic predisposition to remodeling of the cardiovascular system and can be observed at normal BP. The course of the disease can be predicted by the weight of the myocardium and degree of LV hypertrophy in patients with EH [6,8,9].

Our results indicate that the major preclinical signs of LV hypertrophy include morphofunctional changes in the myocardium and remodeling of the vascular system.

TABLE 1. Echocardiography Parameters in Relatives of Patients with Familial EH and Healthy Volunteers ($M\pm m$)

Parameter	Control	Relatives of patients with familial EH
E, cm/sec	75.67±3.98	60.04±4.54*
A, cm/sec	40.05±2.27	49.47±4.96*
E/A	1.84±0.14	1.32±0.17*
LFF, %	30.19±1.37	34.56±2.69*
MILVM, g/m^2	96.75±3.13	104.86±2.13*

Note. E, maximum rate of LV early filling; A, maximum rate of LV late filling; LFF, late filling fraction; MILVM, mass index of the left ventricular myocardium. Here and in Table 2: *$p<0.05$ compared to the control.

TABLE 2. Echocardiography Parameters in Patients with Familial EH ($M\pm m$)

Parameter	Control	Familial EH
E, cm/sec	75.67±3.98	45.34±1.89*
A, cm/sec	40.05±2.27	61.46±2.45*
E/A	1.84±0.14	0.7±0.06*
Ei, cm	8.89±0.58	6.81±0.34*
Ai, cm	3.86±0.33	6.38±0.17*
IRT, msec	62.50±3.78	118.20±5.38*
En	5.75±0.37	3.56±0.14*
LFF, %	30.19±1.37	46.51±1.32*
MILVM, g/m^2	96.75±3.13	52.51±4.96*

Note. Ei, integral of the LV early filling rate; Ai, integral of the LV late filling rate; IRT, isovolumic relaxation time; En, normalized maximum rate of LV early filling.

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