Contractile and Electrical Functions of Rat Heart during Left Ventricular Hypertrophy

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Left ventricular hypertrophy of the hearts in Wistar rats caused by renovascular hypertension prolongs depolarization of epicardial surface of the ventricles and increases the duration of excitation phase in the left ventricular epicardium. Sex-related differences in changes of myocardial contractility were revealed during hypertrophy of the left ventricle caused by renovascular hypertension.

Key Words: *hypertrophy; cardiodynamics; renovascular hypertension; heart; rat*

Left ventricular hypertrophy (LVH) is an adaptive reaction of the heart to sustained increase in systemic blood pressure. Changes in contractile function of the heart during LVH caused by arterial hypertension are diverse [6,9,12] due to hypertrophy of cardiomyocytes [3,12] and fibrosis [4,12].

Our aim was to study cardiodynamics and electrical function of the heart during LVH provoked by renovascular hypertension.

MATERIALS AND METHODS

Experiments were carried out under ether anesthesia on male (n=5) and female (n=6) Wistar rats aging 6-8 months and weighing 174-295 g. The control group comprised normotensive male (n=10) and female (n=13) rats.

Analysis of phasic structure of the cardiac cycle was based on synchronous bipolar ECG (leads from extremities), phonocardiogram, and apexcardiogram recorded before and after the onset of LVH caused by occlusion of the left renal artery. Blood pressure was measured in the abdominal aorta by invasive technique on postoperation week 4. Unipolar electrograms were recorded synchronously from 64 electrodes, which were uniformly located on the ventricular epicardium in rats narcotized with sodium thiopental (100 mg/kg intraperitoneally). The moment of wave entry into the recording points and the moment of restoration of excitability were determined, and the duration of excited state was measured [7].

RESULTS

Occlusion of the left renal artery in rats provoked a pronounced blood pressure rise (Table 1). The weight of the left ventricle (LV) in experimental rats was higher by 26% compared to normotensive controls (ventricular septum included). Moreover, the widths of LV wall and ventricular septum increased by 31 and 24%, respectively.

In hyper- and normotensive rats, the successions of epicardial ventricular depolarization were similar. During the development of LVH, the duration of epicardial ventricular depolarization increased by 2 msec from the normal value (8±1 msec, p<0.01), which was accompanied by widening of *QRS* complex in extremity leads by 3±1 msec (p<0.01).

During the development of LVH, changes in the apex-base gradients of the duration of excited state in LV epicardium were minor: 25±2 and 22±3 msec (p<0.1) in hypertensive rats, 16±6 and 14±5 msec (p<0.05) in normotensive rats. Dispersion of the inter-

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TABLE 1. Hemodynamic and Morphological Indices of LV in Normotensive and Hypertensive Rats (*M*±*m*)

Index	Normotensive rats			Hypertensive rats		
	total (*n*=23)	males (*n*=10)	females (*n*=13)	total (*n*=11)	males (*n*=5)	females (*n*=6)
Systolic pressure, mm Hg	114±6	114±8	113±5	153±15*	157±19*	152±14*
Diastolic pressure, mm Hg	71±7	75±8	69±5	95±15*	104±18*	91±12*
Mean pressure, mm Hg	86±6	88±8	84±4	114±15*	122±18*	111±12*
HR, min^{-1}	353±33	375±34	351±37	365±41	346±53	373±33
LV weight, mg	638±79	672±62	614±83	736±143**	768±131**	721±152**
LV relative weight, %	0.26±0.03	0.25±0.02	0.27±0.03	0.33±0.03*	0.31±0.02*	0.34±0.04*
Thickness of LV free wall, mm	3.4±0.5	3.5±0.6	3.2±0.3	4.4±0.4*	4.5±0.3*	4.3±0.4*
Thickness of interventricular septum, mm	2.5±0.4	2.5±0.5	2.5±0.3	3.1±0.3*	3.4±0.2*	3.0±0.3**

Note. *p<0.01, **p<0.05 compared to normotensive rats.

vals of the excited state in LV epicardium did not significantly differ in hypertensive (18±5 msec) and normotensive (15±5 msec) rats due to lengthening of the duration of excited state on the base (22±3 and 14±5 msec, p<0.01) and apex (25±2 and 16±6 msec, p<0.01) of LV. After the onset of LVH, the following changes were found in ECG: lengthening of QT_{II} (41±6 and 48±9 msec, p<0.01) and QT_{cII} (101±16 and 121±23 msec, p<0.01), which significantly (p<0.05) correlated with the weight of LV (r=0.58 and r=0.64, respectively). A decrease of T_{II} wave amplitude (0.10± 0.05 and 0.08±0.07 mV, p<0.05) was also observed. These shifts were caused by changes in the transmural gradient of the duration of action potential [11-13], rather than changes in its epicardial gradient.

TABLE 2. Chronocardiogram of Contractile Function of Rat Heart before and after Development of LVH (*M*±*m*)

Index	Before hypertrophy			During hypertrophy		
	total (*n*=11)	males (*n*=5)	females (*n*=6)	total (*n*=11)	males (*n*=5)	females (*n*=6)
Length of cardiac cycle, msec	168±19	161±14	174±22	168±24	177±29	160±18
Total systole, msec	90±8	87±6	93±10++	88±13	96±16	82±7*++
Diastole, msec	78±12	74±11	81±13	79±14	81±17	78±13
Mechanical systole, msec	69±8	66±6	72±10++	67±13	75±16	61±5*++
Asynchronous contraction, msec	21±1	21±1	21±1	21±2	21±2	21±3
Isometric contraction phase, msec	15±5	18±3	13±4++	14±2	12±2*	15±2++
Strain period, msec	36±4	38±4	34±4++	34±4	33±4*	36±3
Rapid ejection phase, msec	31±7	30±7	31±8	29±11	34±14	24±5**
Slow ejection phase, msec	24±6	19±2	28±5+	26±10	30±13**	22±2**
Ejection period, msec	54±9	49±7	59±7++	54±15	64±18**	46±7*++
Relaxation period, msec	40±6	42±6	37±5	37±6	38±6	36±6
Rapid filling phase, msec	12±3	11±2	12±4	12±3	13±4	11±2
Filling period, msec	31±9	30±9	32±9	35±14	40±20	31±6
Intrasystolic index	0.78±0.07	0.73±0.06	0.83±0.04+	0.79±0.06	0.83±0.06*	0.76±0.05**++
Myocardial strain index	0.40±0.06	0.45±0.05	0.37±0.02+	0.40±0.08	0.35±0.08*	0.44±0.04*++
Mechanical coefficient	1.54±0.33	1.28±0.27	1.76±0.18++	1.64±0.63	2.03±0.77**	1.32±0.22*++
Isovolumetric index	1.04±0.29	1.27±0.28	0.85±0.10+	0.98±0.22	0.84±0.25**	1.10±0.10*++
Early relaxation index	0.52±0.05	0.52±0.05	0.51±0.04	0.48±0.04**	0.48±0.03	0.48±0.04

Note. *p<0.01, **p<0.05 compared to indices before the development of hypertrophy; +p<0.01, ++p<0.05 compared to males.

The mean duration of basic phases and periods of cardiac cycle and indices of myocardial contractile function did not differ before and after the onset LVH (Table 2) excluding the index of early myocardial relaxation. The decrease in this index indicates worsening of diastolic function of the heart. This decrease demonstrated insignificant negative correlation with LV weight (r=-0.32). However, changes in the structure of cardiac cycle during the development of LVH were opposite in males and females (Table 2). In males, phases of isovolumetric contraction and strain were shortened, while the ejection period was prolonged due to widening of the slow ejection phase. In females, the ejection period decreased due to shortening of the rapid and slow ejection phases. As a result, the index of myocardial strain and isovolumetric index increased, while the mechanical coefficient and intrasystolic index decreased in females. The study showed that in normotensive male rats the heart works in a more strenuous mode than in females. During the development of LVH, changes in the structure of cardiac cycle improve myocardial contractility (physiological LVH) in males, but impair this function in females (pathological LVH). The opposite changes in contractility of LV myocardium observed during hypertension in males and females can be explained by different influence of sex hormones mediated via the rennin-angiotensin system related to autonomic nervous system [1,2] on the regulation of blood pressure and morphogenetic processes during the development of LVH [5,8,10,14] accompanying adaptation of the heart to enhanced load.

Thus, LVH caused by renovascular hypertension does not affect the succession of depolarization of epicardial surface of the ventricles of Wistar rats, but increases its duration (by 25-30%) and prolongs the intervals of excitation in LV epicardium. Despite similar degree of LVH induced by renovascular hypertension, changes in contractile function of the myocardium were opposite in males and females, which was probably caused by different rate of LVH development.

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