Specific Function and Morphology of the Right Ventricle of the Heart during Ischemic Injury of the Left Ventricle

M. L. Blagonravov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 145, No. 4, pp. 392-394, April, 2008
Received October 30, 2007

Focal ischemia of the left ventricular myocardium was modeled by surgical ligation of the descending branch of the left coronary artery at the junction of the lower and middle thirds of this artery in anesthetized rabbits. Contractility and morphological characteristics of the right ventricular myocardium were evaluated 24, 72, and 120 h after treatment. Significant morphofunctional changes in the right ventricle manifested in the development of severe extracellular edema and increase in the area of damaged and destroyed myofibrils. However, the actual and maximum intraventricular pressure remained unchanged under these conditions. The degree of cardiomyocyte apoptosis increased on day 1, but returned to normal in the follow-up period. Our study demonstrated high sensitivity of the right ventricle to left ventricular dysfunction and early activation of compensatory mechanisms.

Key Words: *right ventricle; left ventricle; myocardium; ischemia; apoptosis*

Complex interrelations between the left and right heart are mediated by morphological, biochemical, and functional mechanisms. For example, overload of the right heart affects contractility and structure of the left ventricle. The observed changes are more significant compared to those described in direct damage to the left ventricle [2].

Left ventricular dysfunction is accompanied by impairment of systolic function and increase in hemodynamic load of the right ventricle (RV). Clinical and experimental observations showed that these changes contribute to dysfunction and remodeling of RV [5-8]. Our previous experiments showed that cardiac overload in the early period of hypertension is followed by morphofunctional reconstruction of both ventricles [1,3].

Here we studied the morphology of RV tissue during ischemic injury of the left ventricular myocardium.

Department of General Pathology and Pathophysiology, People's Friendship University of Russia, Moscow, Russia. ***Address for correspondence:*** blagonravovm@mail.ru. M. L. Blagonravov

MATERIALS AND METHODS

Experiments were performed on male Chinchilla rabbits weighing 2.5-3.0 kg. Focal ischemia of the left ventricular myocardium in anesthetized animals was induced by surgical ligation of the descending branch of the left coronary artery at the junction of the lower and middle thirds of this artery. Study was conducted 24, 72, and 120 h after treatment. The control group included intact rabbits. Each functional examination was performed on 5 animals from the group. Morphological study was performed on samples from 2 animals.

Contractile activity of RV was measured in a Mikard hardware-and-software device (computer, analog-digital converter, and electromanometric transducers). This device was calibrated with the water column. RV was catheterized in anesthetized animals. The actual (IPa) and maximum intraventricular developed pressure (IPm, 5-sec compression of the ascending aorta) in RV was measured.

The heart of anesthetized animals was extirpated and perfused with 2.5% glutaraldehyde through

0007-4888/08/1454-0415

the ascending aorta for a morphological study of the RV myocardium. Papillary muscles of RV were excised and treated routinely. Tissue samples were embedded into Epon and araldite. Semithin sections were prepared on a Riechert-Jung-Ultracut microtome and stained as described elsewhere [4]. RV samples were examined under a Nicon Eclipse E-400 light microscope (×1000). Quantitative measurements were based on a morphometric study. In each experimental series, 30 fields of view were studied using an Avtandilov ocular grid. We evaluated the amount of myofibrils, cell nuclei, collagen, vessels, and destruction sites and volume of the extracellular space. The degree of cardiomyocyte (CMC) apoptosis was estimated by the method developed at the Department of General Pathology and Pathophysiology (People's Friendship University of Russia). We estimated the total number of nuclei and count of free nuclei in the extracellular space or completely destroyed cells. The apoptotic index was calculated as the ratio of the count of free nuclei to the total number of nuclei (%).

The results were analyzed by Student's *t* test. The differences between the means were significant at $p \leq 0.05$. The relationship between individual processes and events was estimated by correlation analysis.

RESULTS

RV IPa significantly increased at the end of day 1. This parameter decreased in the follow-up period, but remained above normal (Fig. 1). It is probably related to increased hemodynamic load of RV due to congestion in the pulmonary circulation. The difference between IPa and IPm in RV significantly decreased on day 1. However, the absolute value of RV IPm in all periods remained above normal.

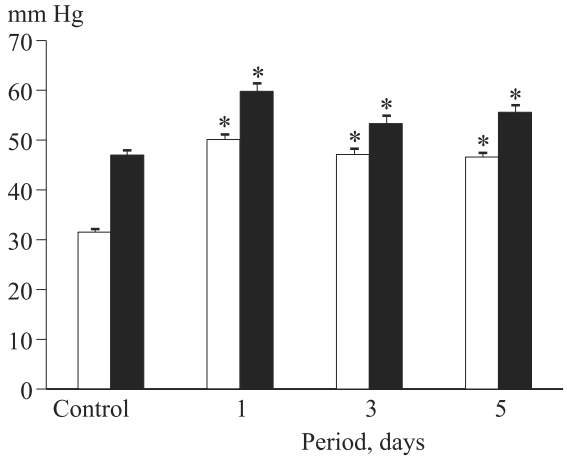

Fig. 1. IPa (light bars) and IPm (dark bars) in RV during focal ischemia of the left ventricle. *$p<0.05$ compared to the control.

It can be hypothesized that ischemic injury to the left ventricle is accompanied by mobilization of reserve capacities in RV. These changes are probably important for cardiac function under extreme conditions. Our results are consistent with the hypothesis on the major regulatory role of RV in cardiac activity [2].

The weight of RV muscles was characterized by wave-like variations. This parameter significantly decreased 24 h postsurgery, returned to normal by the 72nd hour, but decreased again after 120 h (below normal, Table 1). The observed changes are probably related to severe extracellular edema on days 1 and 5. This assumption is confirmed by significant negative correlations between muscle fibers and extracellular spaces in all periods (r=-0.78, day 1; r=-0.63, day 3; r=-0.86, day 5). A progressive increase in the area of damaged and destroyed muscle elements reflects activation of CMC necrosis. However, no correlation was re-

TABLE 1. Morphometry of Semithin Sections from RV ($M \pm m$)

Parameter	Control	Period, days		
		1	3	5
Muscle fibers, vol %	70.27±1.00	67.00±1.29*	72.67±1.17	62.57±1.60*
Nuclei, vol %	1.33±0.20	1.27±0.18	0.77±0.14*	1.00±0.17
Free nuclei	0.13±0.06	0.30±0.09	0.17±0.07	0.23±0.11
Apoptotic index, rel. units	0.08±0.04	0.25±0.07*	0.11±0.05	0.12±0.05
Collagen, vol %	4.33±0.73	4.83±0.58	3.60±0.52	6.50±0.76*
Vessels, vol %	5.87±0.84	1.90±0.45*	2.07±0.54*	0.9±0.2*
Destruction sites, vol %	0.60±0.21	2.47±0.32*	1.77±0.29*	4.13±0.58*
Extracellular space, vol %	17.60±0.95	22.53±1.14*	19.13±1.02	24.90±1.44*

Note. *$p<0.05$ compared to the control.

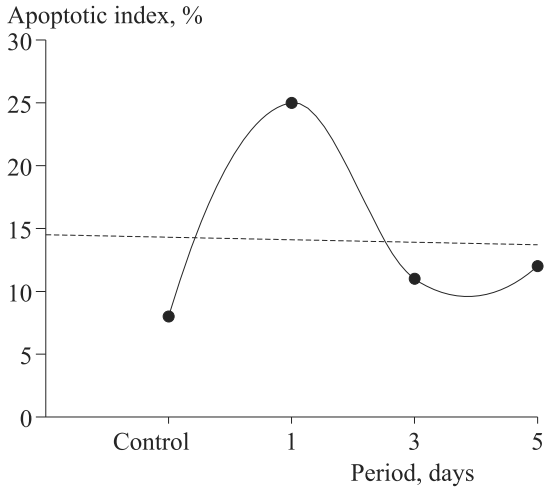

Fig. 2. CMC apoptosis in RV after ischemic injury of the left ventricle. Dotted line: trend for the apoptosis index.

vealed between muscle fibers and destruction sites. Although the severity of destructive processes in the RV myocardium increases, the total volume of muscle elements remains unchanged under these conditions.

It should be emphasized that collagen content in the RV myocardium significantly increases 120 h after modeling of left ventricular ischemia.

Apoptosis in RV sharply increased by the end of day 1, but decreased in the follow up period. We revealed only a tendency toward the increase in this parameter compared to the basal level (Fig. 2). Probably, the immediate response of RV to cardiac injury is the increase in CMC apoptosis. The mechanisms suppressing apoptosis are activated at later stages, since excess death of myocardial cells (apoptosis or necrosis) has a negative effect on the morphofunctional state of RV.

Our results indicate that serious structural changes in the RV myocardium occur during the initial stage of left ventricular ischemia. Morphological reconstruction results from hemodynamic overload of RV, which accompanies a decrease in pump function of the ischemic left ventricle. The increase in the actual and potential working capacity of RV and normalization of CMC apoptosis on day 3 can be considered as activation of the early compensatory mechanisms.

REFERENCES

1. M. L. Blagonravov and V. A. Frolov, *Byull. Eksp. Biol. Med.*, **140**, No. 8, 133-135 (2005).
2. T. A. Kazanskaya and V. A. Frolov, *Right Ventricle of the Heart* [in Russian], Moscow (1995).
3. V. A. Frolov, G. A. Drozdova, P. Rieger, and M. L. Blagonravov, *Byull. Eksp. Biol. Med.*, **137**, No. 3, 249-252 (2004).
4. P. Anthony, Agnese di Sant, L. Karen, and J. De Mesy, *Am. J. Clin. Path.*, **81**, No. 1, 25-29 (1984).
5. G. B. Bleeker, P. Steendijk, E. R. Holman, *et al.*, *Heart*, **92**, Suppl. 1, i14-i26 (2006).
6. M. J. Faber, M. Dalinghaus, I. M. Lankhuizen, *et al.*, *Am. J. Physiol. Heart Circ. Physiol.*, **291**, No. 4, H1580-H1586 (2006).
7. J. K. Hon, P. Steendijk, H. Khan, *et al.*, *Acta Physiol. Scand.*, **172**, No. 2, 97-106 (2001).
8. M. Kret and R. Arora, *J. Cardiovasc. Pharmacol. Ther.*, **12**, No. 1, 5-14 (2007).