Pathomorphology of Myocardial Circulation: Comparative Study in Increased Left or Right Ventricle Afterload

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Comparative study of pathomorphology of myocardial circulation under conditions of increased afterload of the left or right ventricles showed similar changes. All compartments of the coronary bed were plethoric, capillary blood stasis and perivascular edema, more pronounced in arterial vessels, were detected in both cases. These changes equally involved both ventricles and the ventricular septum. Significant differences consisted in local increase in the density of functioning capillaries. The increase was the maximum in hemodynamically overloaded ventricle and ventricular septum, presumably due to increase of their contractile activity. The density of functioning capillaries in the intact (*vs.* pressure overloaded) ventricle also increased, but to a lesser degree, which could be due to systemic neurohumoral effects. If increased afterload was complicated by the development of heart failure, circulatory disorders in the myocardium progressed. Significant increase in the density of functioning capillaries in all cardiac compartments indicated decreased vascular tone and exhaustion of coronary reserve. This was paralleled by a sharp arterial plethora in case of increased afterload of the left ventricle and sharp blood stasis in the microcirculatory bed in case of increased right ventricle afterload. Reduction of effective perfusion pressure in the presence of coronary dystonia can cause coronary insufficiency and myocardial ischemia in case of increased right ventricle afterload.

Key Words: *pathomorphology; myocardial vessels; afterload; left ventricle; right ventricle; heart failure*

Increased afterload (pressure load) observed in vascular hypertension of different genesis can be complicated by the development of acute cardiac failure. Coronary circulation plays an important role in the mechanisms of heart adaptation to increased load and in the pathogenesis of heart failure. The hemodynamic conditions modulating bloodflow in the myocardium are different in systemic and pulmonary hypertension. This fact prompts comparison of myocardial circulation in increased afterload of cardiac left (LV) or right ventricles (RV).

The aim of this study was morphofunctional analysis of myocardial circulation in increased LV or RV afterload and detection of changes prognostically unfavorable for acute heart failure.

MATERIALS AND METHODS

The study was carried out on guinea pigs (500-700 g) under conditions of open chest and jet ventila-

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tion of the lungs. Cardiovascular function was evaluated by ECG, pressure in the aorta and cardiac ventricles, and intraventricular pressure first derivative (dP/dt). The parameters were recorded and processed using a device based on a PC and a Mingograf-82 polycardiographer. Increased afterload was simulated by ligation of the ascending aorta or pulmonary artery trunk, which was paralleled by a 100% elevation of systolic pressure in the heart ventricles in comparison with the initial level. The duration of vascular stenosis was 30 min.

The animals were divided into 5 groups. Group 1 (n=8) were controls subjected to a complete complex of instrumental and surgical interventions, including forced ventilation of the lungs, opening of the chest, and ventricular catheterization, but no vascular stenosis reproduction. In groups 2 and 3 (15 animals each), stenosis of the aorta or pulmonary artery was not aggravated by the development of irreversible heart failure. In groups 4 and 5, stenosis of the aorta (n=3) or pulmonary artery (n=4) was aggravated by the development of heart failure with lethal outcome within the first 30 min.

Directly after the experiment, the hearts were resected and longitudinally dissected into halves, one of which was fixed in 10% neutral formalin buffered after Lilly and embedded in paraffin. Longitudinal serial sections (5 μ) were stained with hematoxylin and eosin, Schiff's reagent (with amylase control) and with iron hematoxylin after Regaud. Ventricular septum (VS) and lateral walls of LV and RV were examined under a microscope. Functioning capillaries in a visual field were counted in preparations stained with hematoxylin and eosin at standard magnification (×600) and converted for 1 mm^2 myocardial section. The data were processed statistically using Student's t test.

RESULTS

The morphology of intramural arteries and veins and of myocardial capillaries in general corresponded to that in health [9,10]. The data on the type and severity of circulatory disorders in the myocardium under conditions of increased afterload are presented in Tables 1 and 2.

TABLE 1. Pathomorphological Types of Circulatory Disorders in the Arterial Compartment of Myocardial Vascular System in Afterload Increase

Disorders	Aortic stenosis			Pulmonary artery stenosis		
	RV	LV	VS	RV	LV	VS
Plethoric arteries						
control	+	—	—	+	—	—
stenosis	+	++	++	++	++	++
steniosis+HF	+++	+++	++	+	++	+
Perivascular arterial edema						
control	+	+	+	+	+	+
stenosis	++	++	++	++	++	++
steniosis+HF	++	+++	++	+++	+++	+++
Arterial thrombosis						
control	—	—	—	—	—	—
stenosis	—	—	—	—	—	—
steniosis+HF	—	—	—	—	—	—
Plasma imbibition of arterial wall						
control	—	—	—	—	—	—
stenosis	—	+	—	+	—	—
steniosis+HF	—	+	—	+	+	—
Damage to arterial wall smooth muscle cells						
control	—	—	—	—	—	—
stenosis	—	+	—	+	+	+
steniosis+HF	—	+	—	+	++	—

Note. Here and in Table 2: '--': no changes or solitary changes; "+": slight changes; "++": moderate changes; "+++": pronounced changes. HF: heart failure.

Disorders of myocardial circulation in aortic stenosis were characterized primarily by plethora of all compartments of the vascular system and by erythrocyte aggregation with the development of blood stasis in the capillaries. These changes were moderate and involved largely the LV and VS. Regaud staining showed solitary damaged smooth-muscle cells in the tunica media of the LV intramural arteries. Plasma imbibition of the walls of a small part of LV arteries was detected in the preparations incubated with amylase and stained with Schiff's reagent. The increase in vascular permeability was paralleled by perivascular edema, which was more pronounced in the arterial compartment of the coronary bed. The density of functioning capillaries increased in comparison with the control: 1.7 times in RV, 2.7 times in LV, and 2.6 times in VS (Fig. 1, *a*, *1*).

Intravascular changes in pulmonary artery stenosis presented by moderately plethoric vessels and blood stasis in myocardial capillaries. Damaged smooth-muscle cells and plasma imbibition of intramural arterial walls were rarely detected, mainly in the RV. Perivascular edema was more pronounced for arteries and less so for veins. The density of functioning capillaries increased in comparison with the control: 3.5 times in RV, 1.8 times in LV, and 5-fold in VS (Fig. 1, *b*, *1*).

Hence, comparative study of the pathomorphology of myocardial circulation in acute increase of the LV or RV afterload showed in general similar changes. All compartments of the coronary bed were plethoric, blood stasis in myocardial vessels, and perivascular edema, more pronounced for the arteries, were observed in both cases. These changes were moderately pronounced and equally involved the LV, RV, and VS.

Simulation of aortic or pulmonary artery stenosis was associated with increased density of functioning capillaries in the myocardium, this indicating intensification of coronary bloodflow. Changes in the myocardial bloodflow are determined by several factors: oxygen consumption by the myocardium, coronary perfusion pressure, extravascular compression force, and neurohumoral factors [3,8,11]. Oxygen consumption by the myocardium increases during intensification of its work, this increase being mainly responsible for the increase in the number of functioning capillaries in hemodynamically overloaded ventricle: in LV in aortic stenosis and in PV in pulmonary artery stenosis. A similar increase in the density of functioning capillaries was detected in VS during LV and RV afterload. Since blood supply sources of VS and both cardiac ventricles are common [4,5], the increase

TABLE 2. Pathomorphological Disorders of Circulation in the Venous and Capillary Compartments of the Myocardial Vascular Network under Conditions of Increased Afterload

Disorders	Aortic stenosis			Pulmonary artery stenosis		
	RV	LV	VS	RV	LV	VS
Plethoric veins control						
stenosis	+	++	++	++	++	++
steniosis+HF	+	++	++	++	++	++
Perivascular venous edema						
control	—	—	—	—	—	—
stenosis	+	+	+	+	+	+
steniosis+HF	+	++	++	++	+	++
Venous thrombosis						
control	—	—	—	—	—	—
stenosis	—	—	—	—	—	—
steniosis+HF	—	—	—	—	—	—
Plethoric capillaries						
control	+	+	+	+	+	+
stenosis	++	++	++	++	+	++
steniosis+HF	++	++	++	++	++	++
Blood stasis in capillaries						
control	—	—	—	—	—	—
stenosis	+	++	++	++	++	++
steniosis+HF	++	++	++	+++	+++	+++

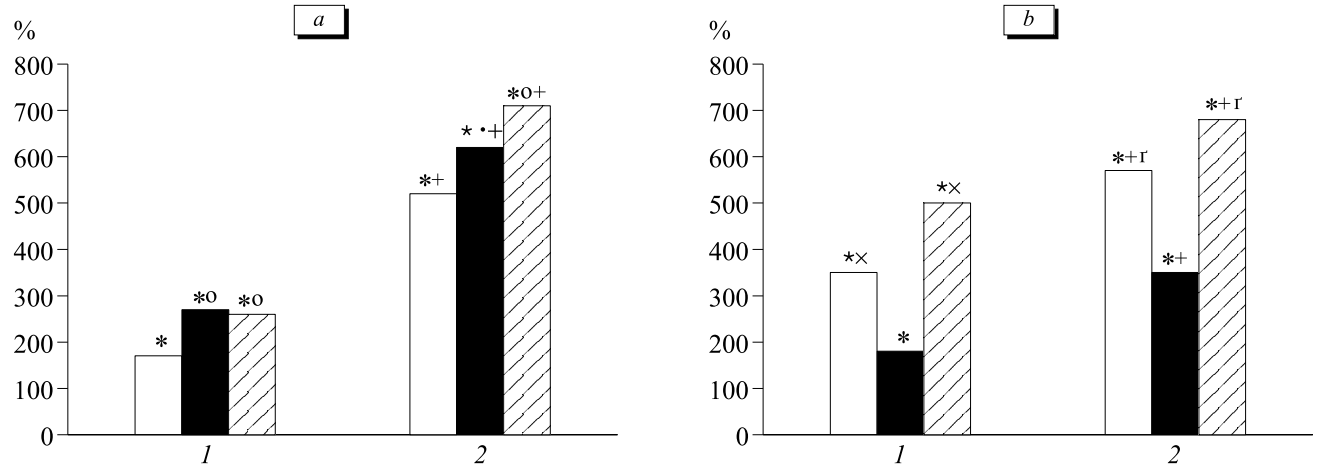

Fig. 1. Changed density of functioning capillaries in the myocardium in aortic (*a*) and pulmonary artery (*b*) stenosis. Ordinates: density of functioning capillaries (control values are taken for 100%). *1*) increase of afterload without development of heart failure; *2*) increase of afterload with development of heart failure. Light bars: RV; dark bars: LV: cross-hatched bars: VS. $p<0.001$ compared to: *control, +increased afterload without heart failure; $p<0.05$ compared to: °RV, ×LV.

in the number of functioning capillaries in VS can be caused by increased bloodflow in the coronary artery basin, common with the functionally overloaded ventricle. However, experimental studies with the use of radioactive microspheres showed that coronary bloodflow changed in strict accordance with changes in the regional myocardial contractility [11,12]. Hence, the increase in the density of functioning capillaries in VS is caused primarily by its increased contractility in simulation of aortic or pulmonary artery stenosis. This conclusion is in line with modern concepts on the important role of VS in the maintenance of the pumping function of LV and RV [4].

The density of functioning capillaries in the myocardium of intact (*vs.* pressure-overloaded) ventricle is increased, but less so in both simulated conditions: in RV in aortic stenosis and in LV in pulmonary artery stenosis. This is presumably caused by systemic neurohumoral effects, among which arterial hypoxia and the sympathoadrenal system are traditionally considered to play an important role. Reduced oxygen tension in the arterial blood leads to reduction of the tone of resistive myocardial vessels and development of hyperemia. The interaction between catecholamines and β_2-adrenergic receptors in the coronary vessels causes their dilatation and intensification of myocardial bloodflow [3,8]. The presence of arterial hypoxia in hemodynamic conditions associated with increased afterload was demonstrated not once in experimental and clinical studies [1,6,13]. We demonstrated an increase of the sympathoadrenal activity in experimental stenosis of the aorta or pulmonary artery previously [7]. Hence, arterial hypoxia and adrenergic effects can promote the increase in the density of functioning capillaries in the myocardium in both simulated conditions. One more mechanism of myocardial bloodflow increase in stenosis of ascending aortic lumen is a sharp increase of coronary perfusion pressure; this mechanism is more significant for RV due to the systolodiastolic pattern of its blood supply [3,4,8].

When aortic stenosis was aggravated by the development of heart failure, sharply pronounced plethora of intraorgan arteries and arterioles was observed. Venous and capillary plethora, erythrocyte aggregation, and blood stasis were moderate. Clots were detected in the lumen of some LV veins. Solitary small focal hemorrhages were detected in some cases. Damaged smooth-muscle cells and plasma imbibition of the vascular wall were detected in just a small part of intramural LV arteries. Pronounced perivascular edema of arterial and arteriolar zones was observed in all heart compartments, particularly in the LV and VS. Moderate perivascular edema was observed in the venous and capillary bed. The density of functioning capillaries increased significantly in comparison with the control: 5.2 times in RV, 6.2 times in LV, and 7.1 times in VS (Fig. 1, *a*, *2*).

When pulmonary artery stenosis was aggravated by heart failure, intravascular changes were characterized by plethora, sharply pronounced blood stasis in myocardial capillaries, and thrombosis of solitary capillaries. Hemorrhages were rare, but in some cases had large focal pattern. Damaged smooth-muscle cells and plasma imbibition of intramural arterial walls were detected. The increase of vascular permeability was paralleled by the development of pronounced perivascular edema, particularly of the arterial and arteriolar zones. The density of functioning capillaries increased significantly in

comparison with the control: 5.7 times in RV, 3.5 times in LV, and 6.8 times in VS (Fig. 1, *b*, *2*).

Hence, when the afterload increase is paralleled by the development of heart failure, the severity of circulatory disorders in the myocardium augments. A significant increase in the density of functioning capillaries in all compartments of the heart indicates reduced tone of resistive vessels and exhaustion of the coronary reserve. Low tone of arterioles and high blood pressure in the coronary arteries in aortic stenosis result in a sharp arterial plethora. Inhibited blood outflow from the coronary veins because of high pressure in the right atrium in pulmonary artery stenosis is associated with pronounced blood stasis in the microcirculatory network, which is usually regarded as an extreme manifestation of the adaptive mechanisms, underlying the regulation of organ circulation [2]. Reduction of effective perfusion pressure (pressure difference in the aorta and right atrium) in the presence of vascular dystonia can cause the appearance of coronary insufficiency and myocardial ischemia in case of RV afterload increase [3,4]. Neurohumoral changes detected previously in stenosis of the aorta or pulmonary artery complicated by heart failure (desympathization of the myocardium and increased specific significance of the adrenal component in the structure of the sympathoadrenal effects on the heart) [7] can promote the above-listed disorders in coronary circulation.

We conclude from these results that disorders in myocardial circulation play a more important role in the pathogenesis of acute heart failure under conditions of increased in RV afterload compared to LV afterload.

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