Hemodynamic Reactions in the Acute Phase of Massive Pulmonary Embolism

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Massive pulmonary embolism is accompanied by the differences between a decrease in systemic and peripheral blood flow and imbalanced blood ejection from the ventricles. The results of the study suggest an association of these hemodynamic responses with redistribution of blood outflows from systemic veins whereby the relative proportion of blood outflowing to the right atrium decreases and that of blood outflowing to the left atrium increases via systemic-pulmonary collaterals.

Key Words: *experimental massive pulmonary embolism; hemodynamics; collateral circulation*

About one-third of patients with massive pulmonary embolism (MPE) die within 1 h of its onset [5]. One reason why no substantial reduction of case fatality rates has been achieved in this condition is insufficient knowledge of the pathophysiology of hemodynamic disturbances [5]. In clinical practice it is impossible to assess the state of the cardiovascular system within the first few hours of the disease because many patients are admitted to hospital later, and the number of parameters recorded in such a condition is limited, since any examination must be undertaken in strict accordance with the established indications for it. The right heart and pulmonary circulation are examined by angiopneumography, perfusion scanning of lungs, and cardiac catheterization.

The purpose of this study was to examine hemodynamic reactions in the systemic and pulmonary circulation in dogs during the first hours of MPE.

MATERIALS AND METHODS

A total of 50 mongrel dogs weighing 15-20 kg were used. They were premedicated with promedol (10 mg/kg intramuscularly) and anesthetized with sodium thiopental (total intravenous dose 20 mg/kg). Acute MPE was produced as previously [1].

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Group 1 consisted of dogs with closed chest. Group 2 included dogs with open chest artificially ventilated with an oxygen-air mixture (40-80% O_2). The control group consisted of dogs without MPE.

In all the dogs, the heart was catheterized via peripheral vessels. Catheters were introduced to record pressure in the aorta, left and right ventricles, and right atrium, and flowmetric sensor was placed in the ascending aorta to record blood flow there. In addition, a flowmetric sensor was placed in the left femoral artery in dogs with closed chest and on the pulmonary trunk in those with open chest. Pressure was recorded with a Pressure Transducer-746 (Siemens-Elema) connected to a Pressure Amplifier-863 (Siemens-Elema). Blood flows were determined with an MF-46 electromagnetic flowmeter (Nihon Kohden). The parameters under study were recorded with a multichannel Mingograf-82 recorder (Siemens-Elema). Zero blood flow was determined in compressed femoral artery, and in the aorta and pulmonary artery it was measured by the level of the diastolic portion of the phasic blood flow curve [3,4]. Peripheral vascular tone (PVT) was estimated by determining the dilation reserve of peripheral vessels during reactive hyperemia [7]. To this end the femoral artery was compressed for 20 sec distal to the installed flowmeter sensor, and blood flow was measured at the peak of reactive hyperemia occurring

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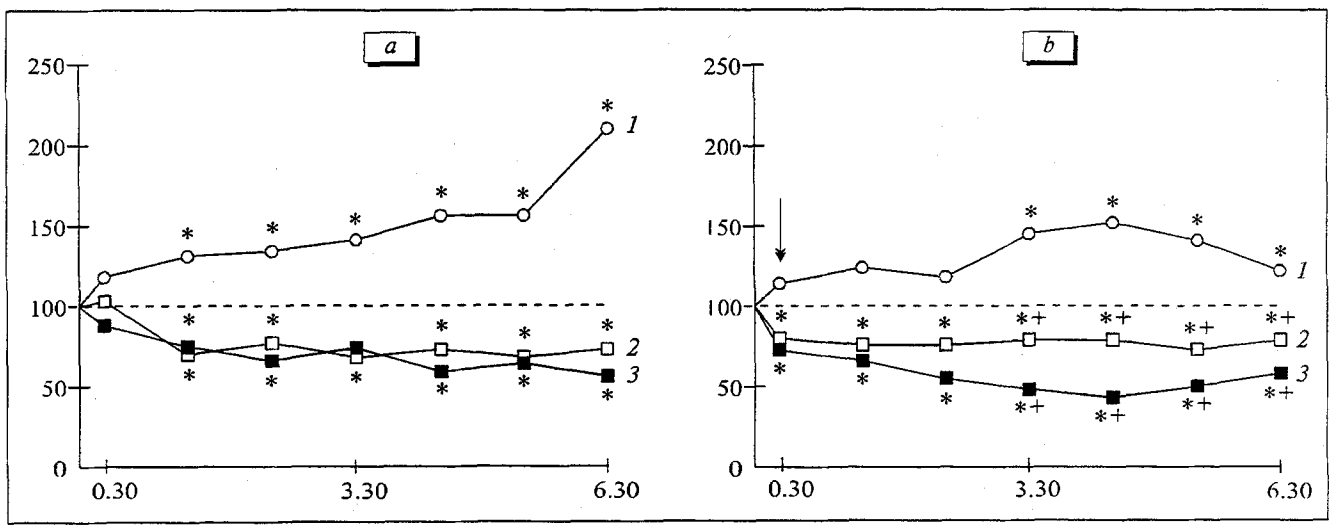

Fig. 1. Temporal variations in systemic and peripheral blood flows and in the tone of somatic vessels recorded in the control dogs (*a*) and experimental dogs with closed chest (*b*). Ordinate: blood flow values in % of the baseline (dashed lines) taken as 100%. *1*) ratio of blood flow at the peak of reactive hyperemia to the initial blood flow in the femoral artery; 2) blood flow in the ascending aorta; 3) blood flow in the femoral artery. Here and in Fig. 2: abscissa: time in hours and minutes after the completion of cardiac catheterization (the time when massive pulmonary embolism was produced is indicated by arrow). $p<0.05$: *compared with baseline; +compared with 2 and 3.

after cessation of compression. The ratio between the reactive and initial blood flows was calculated.

The data were statistically analyzed using Student's *t* test.

RESULTS

In the control group, a progressive increase in PVT was observed in systemic circulation (Fig. 1, *a*) in parallel with a similar magnitude decrease in the aortic and femoral artery blood flows. Since arterial pressure values and cardiac output parameters in the control group remained almost unchanged (Table 1), it was concluded that the blood flows decreased primarily due to increased vascular tone. The proportional decrease in peripheral and systemic blood flow indicated that no redistribution of the systemic blood flow occurred in the control animals.

Comparison of hemodynamic reactions in control (Fig. 1, *a*) and experimental (Fig. 1, *b*) dogs showed similarities as well as substantial differences between them (Fig. 1). PVT values were rising in the two groups in a similar pattern during the first 3-4 h, but later began to fall in the experimental dogs, and continued to increase in the controls so that the intergroup differences became significant by the 6th hour ($p<0.001$). The increase in PVT in experimental dogs was shorter than in the control group and was interpreted as a nonspecific manifestation of the general adaptation syndrome caused by anesthesia, immobilization, and catheterization.

Blood flow in the ascending aorta and femoral artery dropped significantly below the baseline value immediately after onset of MPE (Fig. 1, *b*, *2* and *3*). Since PVT and arterial pressure differed little from the baseline values at that time, the reduction in aortic and femoral artery blood flows was probably due to a weak left ventricle function and a decrease in the circulating blood volume. This suggestion was supported by elevation of right atrium pressure and end-diastolic pressure in the right ventricle (Table 1), which hindered blood drainage from systemic veins and promoted blood deposition there [7]. In MPE dogs, aortic blood flow ceased to decrease, while femoral artery blood flow decreased progressively to a greater extent than in the control. Analysis of cardiodynamic and hemodynamic parameters showed that a decrease in blood flows could result both from weak left ventricular functioning and an increase in PVT in the systemic circulation.

The appearance as well as an increase in the difference between reduction in systemic and peripheral blood flows pointed to blood redistribution during the acute phase of MPE. In principle, these reactions could occur through two mechanisms. The first mechanism involves an increase in blood flow through visceral vessels and a decrease through somatic vessels; in this case, centralization of the circulation will take place, without the differences between right and left ventricle output. The other mechanism involves enhancement of collateral blood flows from systemic to pulmonary vessels with the result that more blood will be ejected from the left ventricle [10,11,14]. As Fig. 2 shows, the blood flow in the pulmonary trunk was initially slightly higher than that in the ascending aorta. This difference was due to

the entry into coronary vessels of some blood ejected by the left ventricle. After MPE was produced, the blood ratio of aortic and pulmonary artery blood flows reversed, and the quantitative difference between these blood flows increased with time.

It should be noted that unlike dogs with closed chest (Fig. 1, *b*), dogs with open chest showed a gradual increase in the aortic blood flow during the initial period of MPE (Fig. 2). This increase was probably due to a progressive decrease in PVT as a result of rapidly developing hypoxemia in the presence of markedly disturbed ventilation-perfusion relationships in artificially ventilated animals with an open chest. An imbalance of a similar magnitude between aortic and pulmonary blood flow during the acute phase of experimental pulmonary embolism was observed in another study [6]. Clinically, quantitative differences between the left and right ventricular outputs are increased in patients with acute MPE [2,12].

The higher left ventricle output was always associated with collateral blood flows in the lungs, i.e., with the entry of blood from systemic into pulmonary vessels via anastomoses between these vessels. Extensive research of collateral circulation in the lungs [8-11,13-16,18,19] revealed the existence of intervessel communications of the following types. First, anastomoses between bronchial and pulmonary vessels at precapillary, capillary, and postcapillary levels have been described in mammals of various species. Second, collaterals exist between bronchial and other vessels in the greater circulation (intercostal, thoracic, esophageal, thyroidal, coronary, pericardial, mediastinal, and some other vessels). Third, bronchopulmonary anastomoses are not the only means of communization between the two circulations: it was suggested that collaterals exist between mediastinal, intercostal, and diaphragmatic vessels, on the one hand, and pulmonary vessels on the other [16,19].

Normally, the collateral blood flow in the lungs amounts to 0.3-3.5% of the left ventricle output, although individual variations can be considerable [8-11,18]. The possibility of augmenting collateral blood flow in cases of pulmonary artery occlusion (PAO) has been under discussion for a long time. It has been established that more blood enters the precapillary and capillary sections of the pulmonary vascular bed from systemic arteries in PAO of long standing (for weeks to months) [14-16,19], contradictory views have been expressed regarding the state of collateral circulation in acute PAO.

The findings concerning this issue can be classified into two groups. On the one hand, blood inflow to bronchial arteries and the magnitude of collateral flow in the pulmonary vascular bed are directly related to changes in pressure and blood flow in the aorta and inversely related to changes in these variables in the pulmonary arteries [7,8,18], precapillary anastomoses between systemic and pulmonary vessels are poorly developed in initially healthy individuals and cannot ensure substantial blood flow in PAO [10,14,16,19], blood inflow to the lungs via systemic arteries decreases within an hour of experimental pulmonary embolism [15], and bronchial blood flow is not enhanced nor bronchopulmonary arterial collateral developed in patients during the first 30 days of pulmonary embolism [16]. On the other hand, it has been shown that the outflow of collateral blood to the left atrium is directly related

TABLE 1. Temporal Variations of Hemodynamic Parameters in the Control and Test Groups with Closed Chest

Parameter	Group	Time (h, min) after cardiac catheterization was completed			
		0.00	0.30	3.30	6.30
Systolic pressure in right ventricle, mm Hg	Control	31±2	29±2	26±1	28±2
	MPE	31±1	70±4*+	59±2*+	55±2*+
End-diastolic pressure in right ventricle, mm Hg	Control	1.5±0.4	1.7±0.9	1.3±0.5	1.1±0.5
	MPE	2.0±0.6	6.8±1.2*+	3.4±1.3	2.9±1.0
Mean pressure in right atrium, mm Hg	Control	-0.5±0.3	-0.7±0.3	-0.6±0.2	-0.6±0.4
	MPE	0.4±0.6	1.6±0.6*	1.5±0.8*	1.8±0.7*
Systolic pressure in left ventricle, mm Hg	Control	151±10	155±12	157±10	142±11
	MPE	196±16*	174±16	178±9	149±14*
Mean pressure in aorta, mm Hg	Control	149±6	147±7	141±5	129±5*
	MPE	144±6	136±7	141±6	120±7*
Heart rate, beats/min^{-1}	Control	197±9	205±7	188±7	194±8
	MPE	188±7	186±8	194±6	191±5

Note. $p<0.05$: *relative to baseline; +relative to control values.

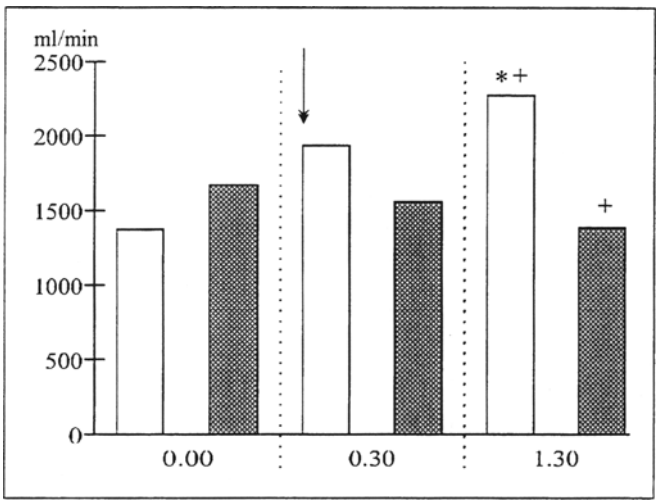

Fig. 2. Temporal variations of aortic and pulmonary artery blood flows during massive pulmonary embolism in dogs with open chest. White bars: blood flow in the ascending aorta; dark bars: blood flow in the pulmonary trunk. $p<0.05$: *relative to baseline; +for the difference between the two blood flows.

to changes in pressure in the right atrium [8,18], well-developed anastomoses normally exist between systemic and pulmonary veins [7], and the outflow of collateral blood to the left atrium is markedly increased in experimental animals with acute PAO [13,18].

In the present study MPE was accompanied by the rise in the systolic and end-diastolic pressures in the right ventricle, a rise of the mean pressure in the right atrium, and moderate falls in the aortic pressure and blood flow (Fig, 1, *b*, and Table 1). From these findings it can be concluded that although in the acute phase of PAO there are no anatomical or hemodynamic conditions for an increase in collateral blood flows at the precapillary level, there are conditions for their increase at the postcapillary level. The redistribution of blood outflow from systemic veins whereby the relative proportion of blood entering the right atrium decreases, while that entering the left atrium via systemic-pulmonary collaterals increases, may account for the growing imbalance between the left and right ventricular outputs during the acute phase of MPE.

The results of this study permit a methodologically important conclusion that the determination of the blood volume ejected one ventricle from that ejected by the other is inappropriate in diseases associated with PAO. Such estimates can probably account for the discrepancy in the results obtained by evaluation of hemodynamic responses during the acute phase of pulmonary embolism, primarily those influencing the total peripheral resistance in the greater circulation. Clinically, the concentration methods are used most commonly to determine cardiac output, most of which record the right ventricular output [3]. Cardiac output in patients with pulmonary embolism is estimated during catheterization of the right chambers of the heart for diagnostic and/or therapeutic purposes. The concept that peripheral blood vessels are markedly spastic and the total peripheral resistance in the greater circulation is elevated in acute pulmonary embolism [5,17] is based on the analysis of systemic arterial pressure and right ventricular output. The wide use of this approach can be explained by the fact that pulmonary artery embolism is rarely classified among the diseases in which substantial differences exist between left and right ventricular outputs. Our findings demonstrate the need for measuring the right or left ventricle output in evaluating hemodynamic reactions in pulmonary or systemic circulation, respectively, in acute pulmonary embolism.

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