Heart Rhythm Disturbances during the Acute Period of Massive Pulmonary Embolism

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We studied the type, incidence, and dynamics of arrhythmia during the acute phase of massive pulmonary embolism complicated or uncomplicated by cardiac insufficiency. Complicated and uncomplicated massive pulmonary embolisms were accompanied by the appearance of single and allorhythmic ventricular extrasystoles, respectively. The rise of the right ventricular pressure to 70 mm Hg was critical for the development of allorhythmia. Allorhythmia started 3-268 sec after attaining the critical ventricular pressure. Heart rhythm spontaneously recovered in 100 and 78% animals with uncomplicated and complicated massive pulmonary embolism, respectively. The duration of paroxysmal allorhythmia varied from 15 sec to 15 min. Electrophysiological processes in the myocardium were normalized with the progression of uncomplicated massive pulmonary embolism: the incidence of single and, especially, allorhythmic extrasystoles decreased, and electrocardiographic parameters returned to normal.

Key Words: *massive pulmonary embolism; arrhythmia*

Little is known about heart rhythm disturbances during pulmonary embolism. Arrhythmia is a severe complication of pulmonary embolism [3] associated with poor prognosis with respect to its surgical treatment [15]. There is disagreement on the type and incidence of arrhythmia in pulmonary embolism [3,9], which is probably related to the absence of data on electrocardiographic parameters that would reflect the severity of embolic occlusion, degree of pulmonary hypertension, and period of observations [9]. Arrhythmia often accompanies massive pulmonary embolism (MPE) [3]. Our previous studies showed that structural and morphological mechanisms underlying impairment of electrophysiological properties of the myocardium differ between MPE complicated and uncomplicated by cardiac insufficiency (CI) [12-14]. We hypothesized that these forms of MPE are accompanied by various heart rhythm disturbances.

Here we studied the type, incidence, and dynamics of arrhythmia during the acute phase of MPE complicated or uncomplicated by CI.

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MATERIALS AND METHODS

Experiments were performed on 37 closed-chest mongrel dogs (15-20 kg) under conditions of natural ventilation. The dogs were premedicated by intramuscular injection of 10 mg/kg promedol and anesthetized by fractional intravenous administration of 20 mg/kg sodium thiopental. Cardiac and vascular catheterization and modeling of acute MPE were performed as described elsewhere [1]. The animals were divided into 2 groups. Group 1 included 21 dogs with uncomplicated MPE, which were euthanized by intravenous injection of sodium thiopental 6 h after the start of MPE. Group 2 included 16 dogs with MPE complicated by CI, which developed over the first 30 min of the experiment.

Heart rate and its variability were studied by 6-lead ECG (I, II, III, aVR, aVL, and aVF) recorded in the supine position using intramuscular limb electrodes on a Mingograf-82 multichannel electrocardiograph (Siemens-Elema) at tape speeds of 50 and 100 mm/sec. To evaluate functional state of the cardiovascular system, blood pressure in the right atrium, aorta,

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and right and left ventricles was measured, first derivative of intraventricular pressure was calculated, and blood flow in the aorta and femoral artery was evaluated. Multichannel recording was performed on a Mingograf-82 device (Siemens-Elema). The results were analyzed by Student's *t* test.

RESULTS

The initial state of animals was characterized by heart rhythm irregularities, in particular, sinus arrhythmia and ventricular extrasystoles (VE, Fig. 1, *a*, *b*, *1*). These functional disturbances are not necessarily associated with heart diseases. Electrophysiological processes in the myocardium are usually evaluated by the incidence and type of arrhythmia. High incidence of extrasystoles and the appearance of early, polytopic, multiple, or allorhythmic extrasystoles indicate electrical instability of the myocardium [2,5].

MPE is usually accompanied by single and allorhythmic VE. Allorhythmia was characterized by regular succession (bigeminal or, more rarely, trigeminal) of extrasystoles and normal sinus beats. Our findings are consistent with published data that bigeminal and trigeminal VE are the only heart rhythm disturbance in dogs with MPE [16]. Clinical observations showed that the acute phase of MPE is characterized by the appearance of VE and allorhythmia [3]. We found no paroxysmal tachycardia, atrial flutter and fibrillation, and ventricular fibrillation typical of patients with MPE [3,15]. This was probably related to the fact that these patients are usually examined at the late stage of MPE and, therefore, have other and/or more severe electrophysiological disturbances. In addition, the preembolic state of patients may be complicated by chronic cardiovascular and lung diseases, which modify electrophysiological properties of the myocardium and contribute to the appearance of those types of arrhythmia, which are absent in experimental animals. Despite this discrepancy between the experimental and clinical observations, we conclude that the acute phase of MPE is characterized by increased electrical instability of the myocardium and heterotopic disturbances in heart rhythm.

VE were found in all animals over the first 30 min of MPE (acute phase, Fig. 1, *a*, *b*, *2*). Electrical instability of the myocardium in group 2 dogs with allorhythmic VE was probably more pronounced than in group 1 animals characterized by the appearance of single VE. Our previous experiments showed that the development of CI during the acute phase of MPE provides structural and morphological basis for the impairment of electrophysiological properties of the myocardium [14].

We revealed an interrelation between right ventricular systolic pressure and the incidence of allorhythmic VE. The rise of the right ventricular pressure to 70 mm Hg was critical for the development of allorhythmia during the acute phase of MPE (Figs. 2 and 3). The latency between this increase in the right ventricular pressure and allorhythmia varied from 3 to 268 sec (average 57±24 sec). This relatively long latency in some animals indicates that metabolic and electrolyte disturbances, but not mechanical tension of the myocardium due to right ventricle dilation, play the major role in the pathogenesis of arrhythmia. The

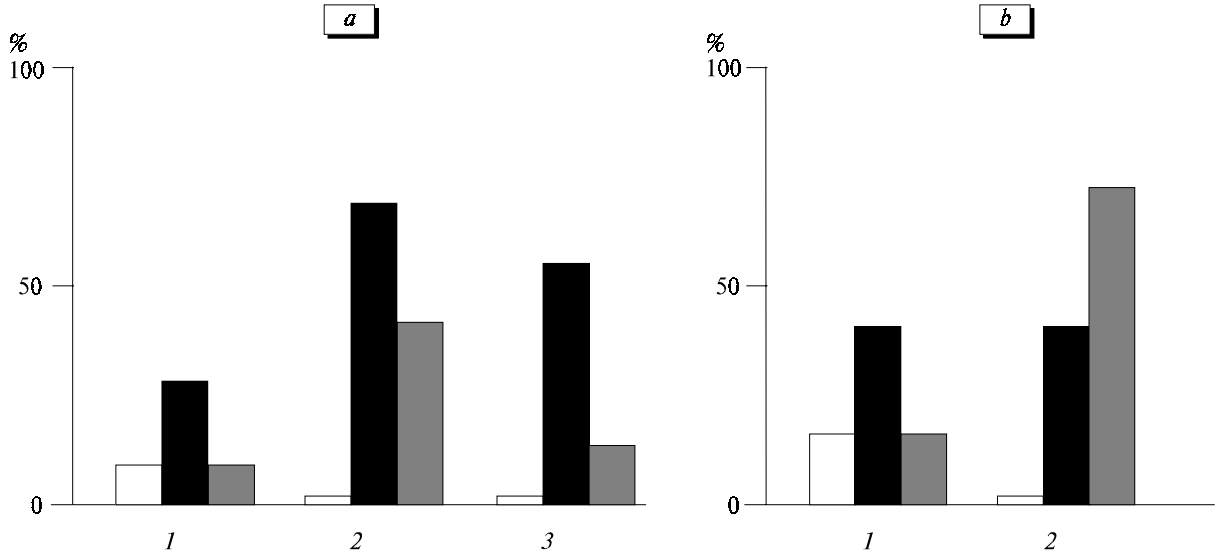

Fig. 1. Incidence of sinus arrhythmia (light bars) and single (dark bars) or allorhythmic (shaded bars) extrasystoles during the acute phase of MPE uncomplicated (*a*) or complicated by cardiac insufficiency (*b*): initial state (*1*), acute phase of MPA (first 30 min of embolism, *2*), and delayed period of MPA (1-6 h, *3*).

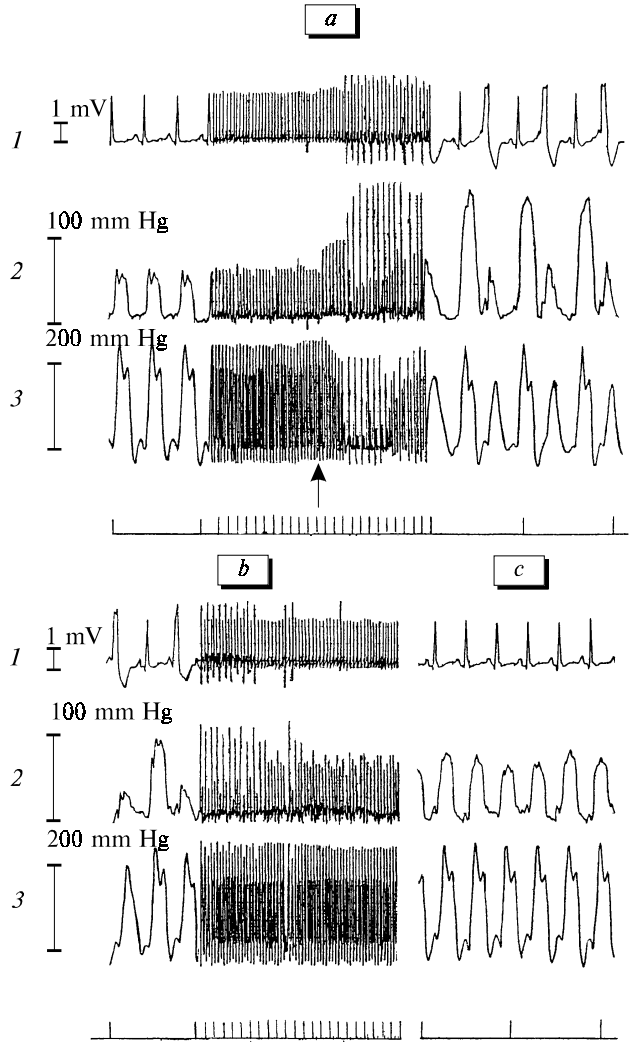

Fig. 2. Development and termination of allorhythmic extrasystoles in the initial phase of uncomplicated MPE: initiation of bigeminy 4 sec after the start of MPE (arrow: administration of the last embolus, *a*); termination of bigeminy (436 sec after the start of MPE, *b*); and normal heart rhythm against the background of stable hemodynamics (494 sec after the start of MPE, *c*). Here and in Fig. 3: ECG, lead II (*1*); right ventricular pressure (*2*); and left ventricular pressure (*3*). Bottom: time mark=1 sec.

development of arrhythmia is not related to reflex reactions, which can be initiated by passage of emboli through the heart and pulmonary vessels or after saltatory rise of blood pressure in the pulmonary circulation.

It is difficult to determine the cause of heart rhythm disturbances, which accompany pathological conditions or disease models in the body. In this case, we evaluate factors and conditions promoting the development of arrhythmia, but not the pathogenetic mechanisms of this disorder. Our experiments showed that hyperfunction and mechanical tension of the myocardium, activation of the sympathoadrenal system, hypercatecholaminemia, arterial hypoxia, insufficiency of energy-forming processes in contractile and conducting cardiomyocytes (CM), their damages, and morphological heterogeneity of the myocardium reduce the arrhythmic threshold of the heart during the acute phase of MPE [7,10-14]. Morphological heterogeneity of the myocardium plays an important role in the development of arrhythmia by the reentry mechanism [4,5,8]. The arrhythmogenic effects of other factors are realized via disturbed ion transport and energy metabolism modulating electrophysiological properties of CM and stimulating ectopic activity [5,8]. These data indicate that changes in electrophysiological properties of CM and impaired conduction of electrical impulses in the myocardium are the major pathogenetic mechanisms of arrhythmia during the acute phase of MPE. Our previous studies showed different contribution of these mechanisms into complicated and uncomplicated MPE [9,15-17]. During MPE uncomplicated by CI, activation of energy-forming processes (in particular, glycolysis) and polymorphism of intramyocardial disturbances provide optimum conditions for reentry, rather than for ectopic activity. During MPE complicated by CI, structural and functional organization of the myocardium is less favorable for the realization of the reentry mechanism. Irreversible damages to conducting and contractile CM, their destruction, and extensive hemorrhages in the intercellular space impair electrical conduction, which suppresses the reentry mechanism. In addition, preserved intercellular contacts are necessary for circulation of excitation waves in the myocardium [4]. Pronounced interstitial edema impairing intercellular contacts probably inhibits reentry during MPE complicated by CI. This assumption is indirectly confirmed by the absence of ventricular fibrillation in our experiments [4,5,8]. We suggest that during MPE complicated by CI, changes in the electrophysiological properties of CM due to impairment of their energy metabolism play the major role in the pathogenesis of arrhythmia. Our previous studies showed that glycolytic processes in conducting and contractile CM, which are closely related to the ion transport system [6], are sharply inhibited during complicated MPE [13,14].

Heart rhythm spontaneously recovered in 100 and 78% animals of groups 1 (Fig. 2) and 2 (Fig. 3), respectively. In group 2 dogs, heart rhythm was normalized against the background of progressive CI. The duration of paroxysmal allorhythmia varied from 15 sec to 15 min.

The incidence of individual and, in particular, allorhythmic VE in dogs with compensated MPE decreased 1-6 h after the start of the experiments (Fig. 1, *a*, *3*). Electrocardiographic parameters were normalized: the amplitude of R waves in all leads increased, signs of right atrium overload and His bundle block-

ade were less pronounced, and the end portion of the ventricular complex was recovered. Therefore, electrophysiological processes in the myocardium were normalized with progression of uncomplicated MPE. The decrease in blood pressure, attenuation of myocardial tension and hyperfunction, shift of myocardial metabolism toward energy-forming processes, and regression of pathomorphological changes in the cardiac conducting system promoted normalization of electrophysiological processes [7,10-14]. It should be emphasized that the incidence of arrhythmia decreased against the background of arterial hyperoxia, hypercatecholaminemia, and heterogeneity of the myocardium. These data attest to an important role of temporal component in arrhythmogenic effects of various factors, but nor their different contribution into heart rhythm disturbances during MPE. The intensity and/or duration of exposure determine the arrhythmogenic effect of these factors. Our results are consistent with changes in the arrhythmic threshold of the heart at various periods of the same disease.

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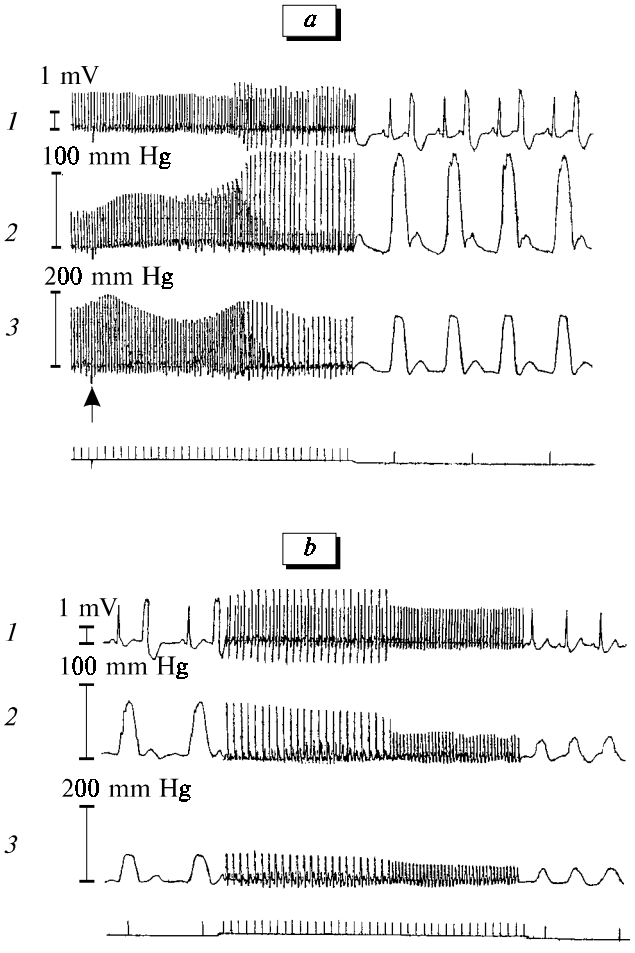

Fig. 3. Development and termination of allorhythmic extrasystoles in the initial phase of complicated MPE: initiation of bigeminy 19 sec after the start of MPE (arrow: administration of the last embolus, *a*); termination of bigeminy against the background of progressive cardiac insufficiency (367 sec after the start of MPE, *b*).

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