Systolic and Diastolic Functions of the Right Ventricle during Massive Pulmonary Embolism

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Massive pulmonary embolism is accompanied by a sharp increase in the contractile activity of the right ventricle. Cardiodynamics during the first 30 min was characterized as subcompensated with impaired relaxation and then progressed to a compensated state (the next 6 h). The initial stage after a sharp increase in right ventricular afterload under massive pulmonary embolism is a critical period in relation to the development of heart failure.

Key Words: *experimental acute pulmonary embolism; cardiodynamics; right ventricle*

Clinical studies showed that one third of patients with massive pulmonary embolism (MPE) died during the 1st hour and two third of these patients died over the 1st day [12], primarily due to right ventricular failure [12,14]. Therefore, studies of the state and functioning of the right ventricle and the mechanisms of right ventricular failure during the first hour after MPE are of considerable importance. These studies can be conducted only under experimental conditions and, therefore, require adequate models, in particular accurate simulation of the localization and severity of damages typical of MPE. Moreover, these models must be reproducible. By contrast to various models of MPE, the model used in our experiments conforms to these requirements [1].

Here we studied the cardiodynamics of the right ventricle during the first 6 h after MPE.

MATERIALS AND METHODS

Experiments were performed on 40 mongrel dogs weighing 15-20 kg without thoracotomy (natural respiration). Premedication was performed by intramuscular injection of 10 mg/kg promedol. Anesthesia was produced by intravenous administration of 20 mg/kg sodium thiopental.

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The experimental group included 20 dogs with MPE not accompanied by heart failure. MPE was modeled as described previously [1]. The control group included 20 dogs without MPE. Euthanasia was performed by intravenous administration of sodium thiopental 6.5 h after heart catheterization.

Catheterization was conducted through peripheral vessels. Blood pressure in the aorta, right atrium, and cardiac ventricles was recorded by external Pressure Transducers 746 (Siemens-Elema) connected to Pressure Amplifiers 863 (Siemens-Elema). The curve of the first derivative of intraventricular pressure was constructed using a Contractility 868 electron differentiator (Siemens-Elema). ECG was recorded by standard limb leads (ECG Amplifier 850, Siemens-Elema). Multichannel recording was performed on a Mingograf-82 device (Siemens-Elema). Indexes of cardiodynamics were determined by polycardiography (simultaneous registration of the above parameters). The data were analyzed using Student's *t* test.

RESULTS

Heart rates in control and experimental animals remained unchanged during the experiment. Therefore, we used uncorrected (not normalized to a standard rate) interval indexes of intraventricular pressure curves

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TABLE 1. Indexes of Cardiodynamics

Index	Determination	Units
Indexes of the intraventricular pressure curve		
EDP	End diastolic pressure corresponding to Q wave on ECG	mm Hg
P_0	Pressure corresponding to $^+$DP on the *dP/dt* curve	mm Hg
PVP	Maximum pressure during ejection	mm Hg
PVP_t	Interval from R wave on ECG to PVP	sec
Indexes of the first derivative of intraventricular pressure curve		
$^+$DP	Maximum *dP/dt*	mm Hg/sec
$^-$DP	Minimal *dP/dt*	mm Hg/sec
^+DP_t	Interval from the moment corresponded to the R wave on ECG to $^+$DP	sec
^-DP_t	Interval from the beginning of the maximum negative wave of the *dP/dt* curve to $^-$DP	sec
$^-DP^-0_t$	Interval from $^-$DP to intersection of the ascending portion of *dP/dt* curve and isoline	sec
$^+DP^-DP_t$	Interval from $^+$DP to $^-$DP	sec
Indexes calculated by curves of intraventricular pressure and its first derivative		
$^+DP/^-DP$		—
$^+DV(^+DP/^+DP_t)$		mm Hg/sec^2
$^-DV(^-DP/^-DP_t)$		mm Hg/sec^2
$^+DV/^-DV$		—
$(^+DP+^-DP)/^+DP^-DP_t$		mm Hg/sec^2
$^+DP/P_0$		sec^{-1}
$^+DP/PVP_t$		mm Hg/sec^2
$PVP/^+DP$		sec
$PVP/^+DP_t$		mm Hg/sec
PVP/PVP_t		mm Hg/sec
PVP^*PVP_t		mm Hg×sec
Phases and periods of cardiac cycle		
Isometric contraction	From R wave on ECG to $^+$DP on *dP/dt* curve	sec
Tension	From Q wave on ECG to $^+$DP on *dP/dt* curve	sec
Ejection	From $^+$DP on *dP/dt* curve to the maximum negative wave of *dP/dt* curve or to the incisura of intraventricular pressure curve	sec
Mechanical systole	From R wave on ECG to the end of ejection	sec
Total systole	From Q wave on ECG to the end of ejection	sec
Diastole	Cardiac cycle minus total systole	sec
Cardiac cycle	The RQ interval on ECG	sec

and its first derivative and the duration of cardiac cycle phases and periods.

MPE was accompanied by a sharp increase in the maximum systolic pressure in the right ventricle (PVP) to 224.6±11.3% (Table 2). Other amplitude indexes of the curves of right ventricular pressure and its first derivative changed similarly (P_0, $^+$DP, and $^-$DP to 206.7±13.5%, 200.0±15.7%, and 257.8±18.7%, respectively). The end diastolic pressure (EDP) in the right ventricle increased to 337.5±58.5%. The increase in PVP was accompanied by an increase in the period of its attainment (PVP_t) to 125.9±8.6%. The lengthening of the ^-DP_t interval was observed in the diastolic portion of the *dP/dt* curve (136.7±12.0%). No changes of interval indexes in the systolic portion of the *dP/dt* curve were found.

Secondary indexes varied with changes in the parameters of right ventricular pressure curves and its first derivative (Table 3). The ratio of $^+$DP/$^-$DP decreased, because $^+$DP increased to a lesser extent than $^-$DP.

TABLE 2. Right Ventricular Pressure and Its First Derivative

Indexes		Time after heart catheterization, h							
		0	0.5	1.5	2.5	3.5	4.5	5.5	6.5
EDP	control	1.5±0.4	1.7±0.9	1.4±0.7	1.7±0.5	1.3±0.5	2.3±0.9	2.3±0.9	1.1±0.5
	MPE	2.0±0.6	6.8±1.2*+	4.5±1.7	3.5±1.1	3.4±1.3	3.6±1.7	2.8±1.4	2.9±1.0
P_0	control	25±1	21±2	21±3	21±2	21±1	21±2	23±1	23±2
	MPE	25±1	51±3*+	45±3*+	43±3*+	42±2*+	40±3*+	39±3*+	39±3*+
PVP	control	31±2	29±2	29±2	27±2	26±1*	27±1	29±1	28±2
	MPE	31±1	70±4*+	62±3*+	60±3*+	59±2*+	57±2*+	53±2*+	55±2*+
^+DP	control	839±95	760±153	730±190	715±236	695±89	710±193	745±163	825±70
	MPE	852±50	1704±134*+	1610±184*+	1635±212*+	1610±172*+	1595±182*+	1446±150*+	1505±95*+
^-DP	control	501±71	565±74	635±92	520±82	492±41	550±54	585±52	557±47
	MPE	565±45	1457±105*+	1296±84*+	1257±94*+	1219±91*+	1188±91*+	1122±97*+	1143±81*+
PVP_t	control	0.078±0.005	0.067±0.004	0.081±0.009	0.081±0.010	0.080±0.005	0.076±0.010	0.077±0.011	0.080±0.005
	MPE	0.074±0.004	0.093±0.006*+	0.083±0.006	0.075±0.005	0.081±0.005	0.076±0.005	0.082±0.007	0.083±0.005
^+DP_t	control	0.057±0.005	0.045±0.004	0.051±0.005	0.049±0.005	0.060±0.005	0.051±0.005	0.053±0.006	0.061±0.005
	MPE	0.057±0.004	0.055±0.004	0.055±0.005	0.051±0.006	0.054±0.004	0.051±0.006	0.054±0.005	0.056±0.005
^-DP_t	control	0.038±0.002	0.039±0.006	0.040±0.003	0.043±0.006	0.042±0.003	0.039±0.005	0.040±0.003	0.047±0.005
	MPE	0.038±0.003	0.051±0.005*	0.043±0.004	0.038±0.004	0.042±0.003	0.037±0.002	0.038±0.003	0.042±0.004
$^-DP^-0_t$	control	0.047±0.004	—	—	—	0.048±0.005	—	—	0.051±0.004
	MPE	0.044±0.004	0.047±0.003	0.041±0.003	0.041±0.003	0.044±0.003	0.041±0.004	0.046±0.004	0.045±0.003
$^+DP^-DP_t$	control	0.127±0.011	0.105±0.013	0.104±0.010	0.111±0.014	0.134±0.011	0.111±0.013	0.109±0.013	0.130±0.011
	MPE	0.113±0.009	0.131±0.009	0.130±0.009	0.125±0.009	0.128±0.007	0.127±0.009	0.121±0.007	0.125±0.007

Note. Here and in Tables 3 and 4. $p<0.05$: *compared with the initial values; +compared with the control.

TABLE 3. Indexes Calculated from Right Ventricular Pressure Curve and Its First Derivative

Indexes		Time after heart catheterization, h							
		0	0.5	1.5	2.5	3.5	4.5	5.5	6.5
$^{+}DP/^{-}DP$	control	1.88±0.19	1.35±0.19	1.12±0.23*	1.26±0.22	1.39±0.13*	1.27±0.30	1.31±0.30	1.60±0.17
	MPE	1.61±0.12	1.17±0.05*	1.23±0.09*	1.32±0.16	1.34±0.11	1.39±0.18	1.37±0.16	1.38±0.10
$^{+}DV\times10^{-4}$	control	1.74±0.37	1.94±0.63	1.76±0.73	1.84±0.90	1.43±0.35	1.76±0.77	1.77±0.69	1.52±0.31
	MPE	1.70±0.18	3.53±0.42*	3.39±0.50*	4.31±1.05*	4.02±0.92*+	4.07±0.95*	3.44±0.64*	3.11±0.35*+
$^{-}DV\times10^{-4}$	control	1.65±0.32	1.84±0.32	1.80±0.23	1.44±0.31	1.35±0.15	1.68±0.28	1.64±0.29	1.45±0.18
	MPE	1.71±0.25	3.53±0.52*	3.41±0.46*	3.72±0.48*+	3.21±0.37*+	3.34±0.34*+	3.25±0.41*+	3.01±0.36*+
$^{+}DV/^{-}DV$	control	1.31±0.19	1.32±0.38	1.13±0.40	1.44±0.55	1.10±0.32	1.21±0.42	1.51±0.71	1.24±0.30
	MPE	1.28±0.22	1.09±0.08	1.04±0.16	1.28±0.36	1.18±0.17	1.45±0.47	1.08±0.14	1.18±0.15
$(^{+}DP+^{-}DP)/$ $^{+}DP-DP_t\times10^{-4}$	control	1.32±0.28	1.47±0.34	1.42±0.32	1.27±0.31	0.98±0.14	1.27±0.27	1.32±0.26	1.19±0.18
	MPE	1.46±0.23	2.70±0.32*+	2.54±0.38*+	2.57±0.35*+	2.42±0.26*+	2.40±0.30*+	2.31±0.26*+	2.27±0.21*+
$^{+}DP/P_0$	control	34.85±2.62	36.85±6.54	34.71±5.98	31.83±6.30	32.52±2.80	33.38±7.25	31.59±6.92	36.74±2.54
	MPE	36.53±3.07	34.85±2.96	36.87±3.88	38.36±4.73	39.12±4.27	43.71±7.20	39.79±4.96	42.07±5.10
$^{+}DP/PVP_t\times10^{-4}$	control	1.22±0.22	1.21±0.32	1.11±0.44	1.09±0.48	0.99±0.23	1.20±0.51	1.23±0.46	1.12±0.20
	MPE	1.26±0.12	2.08±0.25*	2.15±0.30*	2.52±0.50*	2.39±0.41*+	2.42±0.43*	2.13±0.36*	1.99±0.17*+
$PVP/^{+}DP\times10^{2}$	control	3.92±0.34	3.99±0.55	4.60±0.76	4.86±0.87	4.29±0.40	4.87±0.93	4.65±0.80	3.51±0.21
	MPE	3.87±0.26	4.44±0.34	4.32±0.45	4.20±0.38	4.11±0.31	4.05±0.43	4.06±0.34	3.82±0.24
$PVP/^{+}DP_t\times10^{-3}$	control	0.57±0.06	0.62±0.09	0.57±0.10	0.59±0.12	0.49±0.07	0.57±0.10	0.59±0.08	0.50±0.07
	MPE	0.60±0.05	1.38±0.10*+	1.23±0.11*+	1.44±0.22*+	1.33±0.18*+	1.33±0.20*+	1.17±0.12*+	1.11±0.09*+
$PVP/PVP_t\times10^{-3}$	control	0.41±0.04	0.41±0.04	0.37±0.07	0.36±0.07	0.35±0.04	0.39±0.07	0.42±0.06	0.37±0.04
	MPE	0.44±0.03	0.82±0.07*+	0.79±0.06*+	0.87±0.10*+	0.82±0.07*+	0.81±0.08*+	0.73±0.06*+	0.72±0.04*+
$PVP\times PVP_t$	control	2.30±0.19	1.75±0.09	2.15±0.24	2.04±0.18	1.99±0.13	2.01±0.23	2.22±0.33	2.16±0.17
	MPE	2.26±0.16	6.48±0.56*+	5.10±0.43*+	4.44±0.31*+	4.42±0.22*+	4.19±0.22*+	4.06±0.27*+	4.31±0.24*+

TABLE 4. Phases of Functioning of the Right Ventricle

Phases and periods		Time after heart catheterization, h							
		0	0.5	1.5	2.5	3.5	4.5	5.5	6.5
Isometric contraction	control	0.057±0.005	0.045±0.004	0.051±0.005	0.049±0.005	0.060±0.005	0.051±0.005	0.053±0.006	0.061±0.005
	MPE	0.057±0.004	0.055±0.004	0.055±0.005	0.051±0.006	0.054±0.004	0.051±0.006	0.054±0.005	0.056±0.005
Tension	control	0.080±0.005	0.066±0.004	0.072±0.005	0.070±0.005	0.081±0.005	0.072±0.005	0.074±0.006	0.083±0.005
	MPE	0.079±0.004	0.077±0.004	0.077±0.006	0.072±0.006	0.076±0.005	0.072±0.006	0.075±0.006	0.078±0.005
Ejection	control	0.097±0.007	0.090±0.011	0.089±0.010	0.094±0.013	0.098±0.007	0.088±0.011	0.090±0.009	0.096±0.006
	MPE	0.087±0.005	0.092±0.005	0.093±0.006	0.092±0.006	0.094±0.005	0.093±0.005	0.091±0.005	0.094±0.005
Mechanical systole	control	0.150±0.010	0.131±0.013	0.131±0.013	0.136±0.013	0.152±0.010	0.129±0.015	0.131±0.013	0.150±0.011
	MPE	0.143±0.007	0.147±0.007	0.149±0.010	0.143±0.009	0.149±0.008	0.145±0.009	0.145±0.009	0.151±0.008
Total systole	control	0.172±0.010	0.151±0.013	0.151±0.013	0.156±0.013	0.173±0.010	0.149±0.015	0.151±0.013	0.172±0.011
	MPE	0.165±0.007	0.169±0.008	0.170±0.010	0.165±0.010	0.172±0.008	0.166±0.009	0.166±0.009	0.173±0.009
Diastole	control	0.189±0.014	0.173±0.007	0.176±0.013	0.183±0.009	0.242±0.021*	0.180±0.015	0.178±0.014	0.193±0.015
	MPE	0.172±0.013	0.179±0.013	0.170±0.009	0.163±0.010	0.153±0.006+	0.162±0.008	0.169±0.009	0.155±0.008+
Cardiac cycle	control	0.352±0.018	0.312±0.009	0.320±0.014	0.329±0.012	0.406±0.028	0.318±0.017	0.318±0.018	0.359±0.022
	MPE	0.337±0.016	0.350±0.018	0.339±0.015	0.328±0.014	0.325±0.010+	0.328±0.011	0.335±0.010	0.328±0.009

^{+}DV, ^{-}DV, ($^{+}DP+^{-}DP$)/ $^{+}DP^{-}DP_t$, $^{+}DP/PVP_t$, $PVP/^{+}DP_t$, PVP/PVP_t, and $PVP \times PVP_t$ increased to 208.1±24.9%, 207.2±30.6%, 184.2±22.1%, 165.3±19.9%, 229.2±16.6%, 186.4±15.6%, and 286.8±24.7%, respectively. $^{+}DV/^{-}DV$, $PVP/^{+}DP$, and $^{+}DP/P_0$ did not change. The index of $^{+}DP/P_0$ was most stable.

The duration and structure of the cardiac cycle did not change during the first 30 min of MPE (Table 4).

During the next 6 h of uncomplicated MPE, right ventricular PVP slightly decreased but remained above the initial and control values (Table 2). Other amplitude indexes of the right ventricular pressure curve and its first derivative (P_0, ^{+}DP, and ^{-}DP) changed similarly. Right ventricular EDP decreased after 1 h and then did not differ from the initial and control values. Starting from the first hour of MPE, no lengthening of the PVP_t interval was observed. Interval indexes in the systolic and diastolic portion of the *dP/dt* curve did not change significantly.

Changes in the parameters of right ventricular pressure curve and its first derivative affected the dynamics of the secondary indexes (Table 3). The ratio of $^{+}DP/^{-}DP$ did not differ from the initial and control values 2 h after the start of MPE. ^{+}DV, ^{-}DV, ($^{+}DP+^{-}DP$)/ $^{+}DP^{-}DP_t$, $^{+}DP/PVP_t$, $PVP/^{+}DP_t$, PVP/PVP_t, and $PVP \times PVP_t$ remained increased over 6 h of uncomplicated MPE.

The duration and structure of the cardiac cycle did not change over 6 h of uncomplicated MPE (Table 4).

Thus, MPE is accompanied by a sharp increase in contractile activity of the right ventricle. High contractile activity indexes of the right ventricle indicate that the severity of embolic damages in pulmonary vessels is the same throughout the experiment. Over the first 30 min of MPE, the cardiodynamics of the right ventricle is subcompensated with the impairment of relaxation. Delayed relaxation (lengthening of the $^{-}DP_t$ interval) is typical of many heart diseases, including those accompanied by high afterload [2-4, 8,11]. It should be noted that diastolic dysfunction precedes the impairment of myocardial contractile activity [3,4,13]. The delayed relaxation results from disturbances in Ca^{2+} release, insufficient production of macroergic phosphates in cardiomyocytes, and low ATPase activity of contractile proteins [3,5,6,9,10]. Some authors showed that early disturbances in the relaxation processes is due to their high sensitivity to pathological effects leading to accumulation of sarcoplasmic Ca^{2+} and insufficient energy formation in cardiomyocytes [3,5,7]. The sarcoplasmic reticulum plays the major role in the regulation of isometric relaxation [8].

Our findings prove the compensated state of cardiodynamics of the right ventricle from the 1st to the 6th hour of MPE. This is confirmed by normalization of PVP_t, $^{-}DP_t$, and $^{+}DP/^{-}DP$ indexes and a decrease in EDP in the right ventricle. During this period, the right ventricle is assumed to function under static conditions characterized by equilibrium between pathological and compensatory mechanisms (compensation). By contrast, during the first 30 min after a sharp increase in afterload, the right ventricle functions under intermediate conditions characterized by imbalance between these mechanisms, which can be accompanied by various functional disorders. Therefore, the initial stage of MPE is critical for the development of right ventricular failure. This agrees with clinical studies demonstrating high mortality during the first hour of MPE [12,14].

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