TREATMENT OF CANINE ACUTE PULMONARY EMBOLIC SHOCK

—Effects of Isoproterenol and Norepinephrine on Hemodynamics and Ventricular Wall Motion—

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To determine indications for isoproterenol and norepinephrine, the effects of each drug on acute pulmonary embolic shock were compared with those of mechanical occlusion of the descending aorta (AO). In 18 dogs, we measured the changes in the hemodynamics and the ventricular wall motion in experimental pulmonary embolic shock. When the left ventricular systolic pressure decreased to 70 mmHg (shock), dogs were treated with isoproterenol, norepinephrine or AO. At the shock, the difference between the left and right ventricular pressures became negative. The changes in the left and right ventricular septum-free wall diameter (LVD, RVD) resulted in a significant leftward shift of the interventricular septum (IVS), and systolic shortening in LVD was extremely diminished. Isoproterenol administration decreased left and right ventricular end-diastolic pressure (LVEDP, RVEDP), but did not improve the reversion in RVEDP and LVEDP. The leftward shift of the IVS was not restored to normal. Following either norepinephrine administration or AO, the difference between the left and right ventricular pressures was restored to normal. Improvements in left ward shift of the IVS and systolic shortening of each diameter were observed. The similarity of norepinephrine administration to AO suggests that in the treatment of acute pulmonary embolic shock, restoration of systemic pressure for the maintenance of coronary perfusion, may be of primary importance. We concluded that norepinephrine is superior to isoproterenol for improvement of hemodynamics and ventricular wall motion in severe pulmonary embolic shock.

THE incidence of pulmonary thromboembolism in Japan is still lower than that in Western countries but is increasing year after year with the Westernization in life style! This disease may require advanced levels of emergency treatment in the future. The major cause of death in acute pulmonary embolism is shock due to acute right ventricular failure after massive pulmonary

embolism, and the mortality was recently reported to be 32%².

Up to now, in cases of shock due to acute pulmonary embolism, cardiogenic drugs, especially catecholamines, have been frequently used to improve hemodynamics³. Isoproterenol and norepinephrine are the major drugs in use. The effects of these catecholamines are still controversial. Although they have been clinically used, and experimental studies have been performed, only a few systematic studies have been made. To our knowledge, there are no reports that simultaneously evaluated their effects on the right and left ventricular func-

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Fig.1. Instrumentation and Location of Micro-crystal Pairs for Measurement of LVAP, LVD, RVD and RVSL

TABLE I GLOSSARY OF THE TERMS
(in alphabetical order)

AO	: mechanical occlusion of the descending aorta
C	: control value
HR	: heart rate
ISO	: isoproterenol
IVS	: interventricular septum
LVAP	: left ventricular anterior-posterior diameter
LVD	: left ventricular septum-free wall diameter
LVEDP	: left ventricular end-diastolic pressure
LVSP	: left ventricular systolic pressure
max-PH	: maximum pulmonary hypertension
NE	: norepinephrine
RVD	: right ventricular septum-free wall diameter
RVEDP	: right ventricular end-diastolic pressure
RVSL	: right ventricular segment length
RVSP	: right ventricular systolic pressure
S-PH	: shock due to pulmonary embolism

tion in terms of ventricular wall motion with consideration of pericardial preservation which minimizes the effects of ventricular interaction, and with consideration to damage of the ventricular wall.

Under pericardial preservation, we placed ultrasonic crystals on the endocardial surfaces of the bilateral ventricle⁶ in dogs that underwent thoracotomy under anesthesia, and recorded the changes in the hemodynamics and in the wall motion of the bilateral ventricle in experimental acute pulmonary embolic shock. Then, to determine indications for isoproterenol and norepinephrine,

the effects of each drug on acute pulmonary embolic shock were compared with those of mechanical occlusion of the thoracic aorta for the maintenance of coronary circulation^{7,8}

METHODS

1. Experimental Animals

Adult mongrel dogs weighing between 8.4 and 18.7 kg (mean, 12.0 kg) were intravenously anesthetized with sodium pentobarbital (25 mg/kg). Under artificial ventilation (Harvard respirator type 613), a trans-sternal bilateral thoracotomy was made in the fifth intercostal space. To prevent hypoxemia, the animals were ventilated using 30–35% oxygen at a tidal volume of 30 ml/kg and a rate of 15–20 times/minute.

The location and status of the ultrasonic crystal were confirmed at autopsy.

2. Measurement of Hemodynamics, Right- and Left Ventricular Diameters, and Segment Length of the Right Ventricular-Free Wall

Right and left intraventricular pressures were measured using a catheter-tip manometer (PC-350, Millar) inserted via the cardiac apex. Cardiac output (CO) was measured using an electromagnetic blood flow probe placed around the pulmonary arterial trunk after a small pericardial incision (MF-1200, Nihon Kohden). We calculated heart rate (HR) from the recorded cardiac cycles.

Ventricular wall motion was recorded by

Fig.2. Course of Pulmonary Embolic Shock

CO: cardiac output, LVP: left ventricular pressure, RVP: right ventricular pressure, RVP right ventricular pressure, E: lycopodium spores, other abbreviations are same as Table I.

the ultrasonic method (UDM-5, Mediland). Under pericardial preservation, 3 pairs of crystals (5 mm in diameter) were placed on the right and left ventricular endocardial surfaces through each atrial appendage by the previously reported method⁶. Using this method, the right and left interventricular septum-free wall diameters (RVD and LVD) can be measured on a straight line and left ventricular anterior-posterior diameter (LVAP) on a line intersecting it at right angles. In addition, right ventricular segment length (RVSL) was measured using a pair of crystals (2 mm in diameter) inserted into the site slightly toward the anterior wall from the center of the right ventricular free wall along the myocardial arrangement at a 10 mm interval (Fig. 1).

Throughout the course, values were continuously recorded on an 8 channel recorder (RM-85, Nihon Koden), and changes in ventricular wall motion, morphology, and hemodynamics were analyzed.

3. Induction of Pulmonary Hypertension by Pulmonary Embolization and Indices of Shock due to Pulmonary Embolism

To induce pulmonary hypertension, a suspension of lycopodium spores in physiologic-

al saline (50 mg/ml) was repeatedly infused at a volume of 0.5–1 ml via a catheter inserted from the femoral vein into the inferior vena cava immediately caudal to the right atrium. Shock due to pulmonary embolism was considered to have occurred at the point (S-PH) at which right ventricular systolic pressure (RVSP), after increasing from the control value (C) to the maximum value (max-PH), decreased to about 50 mmHg and the left ventricular systolic pressure (LVSP) decreased to about 70 mmHg with an RVSP/LVSP ratio=0.7.

4. Drug Administration and Occlusion of the Thoracic Descending Aorta in Shock due to Pulmonary Embolism

Treatment of shock resulting from pulmonary embolism was initiated at S-PH. Isoproterenol (ISO) was intravenously injected repeatedly at a dose of 16 μ g/kg 1 to 5 times (2 ± 2 times) (mean $\pm$ SD) in 6 animals and norepinephrine (NE) at 8 μ g/kg 1 to 7 times (3 ± 1 times) (mean $\pm$ SD) in 6 animals. In the remaining 6 animals, a cloth tape snare that had been applied in advance was tightened for occlusion of the thoracic descending aorta (AO). LVSP in each group was increased to a value similar to the con-

Fig. 3. Effect of Isoproterenol on Pulmonary Embolic Shock
ISO: isoproterenol administration, other abbreviations are same as Fig. 2.

trol value in order to evaluate the effects of each treatment.

5. Statistical Analysis

The process of the development of shock due to pulmonary embolism and the effects of treatment were compared using the Student's *t* test. The significant level was considered to be $p < 0.05$. All data except drug injection and embolization are presented as mean $\pm$ SE.

RESULTS

1. Hemodynamics and Ventricular Wall Motion in the Process of Production of Pul-

monary Hypertension and in Shock due to Pulmonary Embolism

In the process of the production of pulmonary hypertension by repeated embolization, RVSP increased first from the control value of 32.4 ± 1.3 mmHg to a maximum value of about 63 mmHg (max-PH). CO decreased to about 72% of the control value of 0.97 ± 0.08 l/min, and LVSP to about 85% of the control value of 119.4 ± 3.2 mmHg. With progression of pulmonary hypertension, the right ventricular end-diastolic pressure (RVEDP) increased, and left ventricular end-diastolic pressure (LVEDP) decreased, reaching similar values (about 6.8 mmHg) at the max-PH. Following additional embolization, CO markedly decreased to about 46% of the control value, and both RVSP and LVSP decreased to 49.9 ± 2.2 and 71.1 ± 2.4 mmHg (about 60% of the control value), respectively, showing an RVSP/LVSP of 0.72 ± 0.04 . At this point (S-PH), RVEDP was 16.1 ± 0.7 mmHg, and LVEDP was 6.0 ± 0.3 mmHg; the difference between the left and right ventricular pressures (LVEDP - RVEDP) became negative. Heart rate (HR) slightly decreased during this period (Fig. 2, 6, 7).

At the max-PH, in end-diastole, RVSL did not change from the control value of 10.1 ± 0.7 to 10.2 ± 0.6 mm, and RVD increased from 8.7 ± 1.0 to 10.0 ± 1.1 mm while LVD decreased from 18.9 ± 1.1 to 16.8 ± 1.3 mm. In end-systole, RVSL did not change from 7.9 ± 0.3 to 8.2 ± 0.4 mm, and RVD increased from 5.3 ± 0.8 to 7.0 ± 0.8 mm while LVD decreased from 16.4 ± 1.1 to 14.8 ± 1.3 mm. Both in diastole and systole, extension of the right ventricular free wall and leftward shift of the interventricular septum were apparent. No significant changes were observed in LVAP in diastole or systole. At S-PH, in end-diastole, RVSL increased from 10.2 ± 0.6 at max-PH to 10.8 ± 0.6 mm and RVD from 10.0 ± 1.1 to 13.1 ± 1.2 mm while LVD further decreased from 16.8 ± 1.3 to 14.2 ± 1.4 mm. In end-systole, RVSL increased from 8.2 ± 0.4 to 8.8 ± 0.3 mm and RVD from 7.0 ± 0.8 to 9.9 ± 0.9 mm. On the other hand, LVD decreased from 14.8 ± 1.3 to 13.2 ± 1.2 mm; the value in systole was similar to that in diastole or higher in some animals. LVAP did not change significantly (Fig. 2, 8). At S-PH, the leftward shift of

Fig.4. Effect of Norepinephrine on Pulmonary Embolic Shock
NE: norepinephrine administration, other abbreviations are same as Fig. 2.

the interventricular septum observed at max-PH further increased, and systolic shortening in LVD was extremely diminished. LVAP did not significantly change until S-PH.

2. Changes in Hemodynamics and Ventricular Wall Motion after ISO Administration in Shock due to Pulmonary Embolism

HR markedly increased from the preadministration value of 123.0 ± 18.8 to 144.0 ± 20.0 beats/minute at the time of restoration of LVSP following the ISO administration. LVSP transiently increased to 114.0 ± 21.2 mmHg, and RVSP tended toward increase to 60.2 ± 7.3 mmHg. RVSP/LVSP improved from the preadministration

value of 0.69 ± 0.10 to 0.57 ± 0.10 , but CO did not change significantly from about 49% of the control value to about 54% at the restoration of LVSP following the administration. Both RVEDP and LVEDP decreased, but their difference (LVEDP—RVEDP) remained negative (Fig. 3, 6, 7). The end-diastolic ventricular diameters at the restoration of LVSP were similar to those at S-PH. In systole, only LVAP decreased from 17.8 ± 2.9 mm at S-PH to 15.7 ± 2.7 mm at the restoration of LVSP following the administration (Fig. 3, 8). Following the ISO administration, a marked increase in HR, transient restoration of LVSP to the control value, and decrease in LVEDP and RVEDP

Fig.5. Effect of Aortic Occlusion on Pulmonary Embolic Shock
AO: occlusion of descending aorta, other abbreviations are same as Fig. 2.

were observed, the reversion in right and left ventricular end-diastolic pressures did not improve, and CO did not change significantly. The systolic shortening of LVAP was enhanced, but leftward shift of the interventricular septum was similar to that at S-PH. After LVSP transiently improved to 114 mmHg, right and left ventricular pressures gradually decreased, and the hemodynamics became aggravated. Despite repeated administration, all animals died within 10 min.

3. Changes in Hemodynamics and Ventricular Wall Motion after NE Administration in Shock due to Pulmonary Embolism

HR did not change from the preadministration value of 123.8 ± 18.2 to 131.3 ± 19.0 beats/minute. LVSP increased from 70.5

± 6.5 to 120.7 ± 6.4 mmHg and RVSP from 50.3 ± 3.0 to 75.3 ± 6.5 mmHg. RVSP/LVSP slightly improved from 0.74 ± 0.08 to 0.62 ± 0.05 , and CO increased from about 46% of the control value to about 67%. RVEDP decreased from 16.2 ± 1.0 to 12.7 ± 0.7 mmHg while LVEDP increased from 6.2 ± 0.5 to 11.2 ± 1.4 mmHg, resulting in similar pressures. End-diastolic RVSL decreased from the preadministration value of 10.5 ± 1.3 to 9.6 ± 1.2 mm at the restoration of LVSP, and RVD decreased from 13.6 ± 1.8 to 11.0 ± 2.3 mm while LVD increased from 14.1 ± 2.9 to 16.2 ± 3.2 mm. In end-systole, RVSL decreased from 8.6 ± 0.8 to 7.5 ± 0.9 mm at the restoration of LVSP, and RVD decreased from 10.3 ± 1.1 to 7.7 ± 1.6 mm while LVD increased from 13.1 ± 2.4 to

Fig. 6. Hemodynamic Changes of Therapeutic Interventions [1] (Mean $\pm$ SE)
 CO: cardiac output, HR: heart rate,
 RVSP/LVSP: RVSP-LVSP ratio, (p vs control value in Control, and p vs S-PH in other interventions.)

14.2 ± 2.9 mm. The increase in CO and the decrease in RVEDP following the NE administration show improvements in hemodynamics. In addition, the improvements in leftward shift of the interventricular septum and systolic shortening of each diameter such as LVD were not observed with ISO. In this group, as long as the NE administration was repeated, the hemodynamics remained stable (Fig. 4, 6, 7, 8). However, after discontinuation of NE, the hemodynamics gradually deteriorated to the state at S-PH, and the animals did not survive.

4. Changes in Hemodynamics and Ventricu-

lar Wall Motion after AO in Shock due to Pulmonary Embolism

HR did not change. CO increased from about 45% of the control value before AO to about 62% at the restoration of LVSP. RVSP increased from the pre-AO value of 51.2 ± 4.4 to 68.3 ± 5.6 mmHg following AO, resulting in decrease in RVSP/LVSP from 0.73 ± 0.08 to 0.46 ± 0.09 . RVEDP decreased from 16.5 ± 0.9 to 12.0 ± 2.3 mmHg while LVEDP increased from 6.1 ± 0.5 to 9.8 ± 1.3 mmHg. End-diastolic RVSL decreased from 10.7 ± 1.1 to 9.8 ± 0.9 mm and RVD from 13.1 ± 1.9 to 10.5 ± 2.1 mm, and LVD increased from 14.4 ± 2.9 to 16.7 ± 2.9 mm. In end-systole, RVSL slightly decreased from 8.9 ± 0.6 to 8.1 ± 0.6 mm and RVD from 10.0 ± 1.4 to 7.1 ± 1.4 mm while LVD increased from 13.0 ± 2.7 to 14.6 ± 2.9 mm. LVAP in systole or diastole did not change following AO. Changes in hemodynamics following AO were similar to those following the NE administration. The leftward shift of the interventricular septum improved, and improvements in systolic shortening similar to those after NE administration were observed (Fig. 5, 6, 7, 8). After the release of AO, the hemodynamics returned to the pre-AO state and then gradually deteriorated, resulting in death in all animals.

DISCUSSION

In shock due to pulmonary embolism, in addition to right ventricular loading, cardiac output and systemic blood pressure are decreased. Therefore, in its treatment, adequate attention should be paid not only to pulmonary circulation but also systemic circulation, left cardiac function and coronary perfusion.

In Western countries, ISO and NE have been the drugs of first choice^{5,9-15}. ISO is considered to dilate the pulmonary vessels and to enhance cardiac contraction⁵, and NE to maintain coronary and cerebral perfusion by constricting the peripheral vessels¹³. However, there have been only a few systematic studies of these drugs. Most of the reports on them evaluated their effects in terms of changes in survival rates or hemodynamics. In the present study, we analyzed in detail not only hemodynamics

Fig. 7. Hemodynamic Changes of Therapeutic Interventions [2] (Mean $\pm$ SE)

LVSP: left ventricular systolic pressure, RVSP: right ventricular systolic pressure, LVEDP: left ventricular end-diastolic pressure, RVEDP: right ventricular end-diastolic pressure, RV: right ventricle, LV: left ventricle. (p vs control value in Control, and p vs S-PH in other interventions.)

but also the wall motion and morphological changes of the bilateral ventricle. Both drugs were administrated by repeated intravenous injection. The function of the bilateral heart rapidly deteriorates after S-PH, thus this method was chosen in order to ensure the rapid appearance of the drug effects.

Salisbury⁷ and Spotnitz et al⁸ reported that AO increases coronary perfusion pressure in right heart failure due to an acute increase in pulmonary vascular resistance, resulting in improved right ventricular contraction and restoration of CO. Notably, Spotnitz et al observed that dogs in shock due to pulmonary embolism showed an LVSP of 40 mmHg,

which is still lower than the LVSP in the present study (70 mmHg). Furthermore, they observed restoration of the hemodynamics following AO of the abdominal aorta by the balloon catheter method⁸. They suggested that this method is applicable during low cardiac output that is not responsive to drug treatment. AO is considered to be one of non-medical methods for improving coronary perfusion.

To observe wall motion and the morphology of the ventricles, pericardial preservation is known to be important in terms of ventricular interference¹⁶⁻¹⁸. With our method⁶, pericardial damage was slight. In addition, at the time of the placement of the flow

Fig.8. Dimensional Changes of Therapeutic Interventions (Mean $\pm$ SE)
 RVSL: right ventricular segment length, RVD: right ventricular septal-free wall diameter, LVD: left ventricular septal-free wall diameter, LVAP: left ventricular anterior-posterior diameter, ED: end-diastole, ES: end-systole. (p vs control value in Control, and p vs S-PH in other interventions.)

probe for pulmonary arterial trunk blood flow care was taken to minimize the effects of the pericardial incision. Our method allows stable measurement of the maximum diameter of the interventricular septum-free wall on one straight line and simultaneous measurement of left ventricular anterior-posterior diameter on a line intersecting it at right angles. As a result, left ventricular centripetal contraction, right ventricular bellows-like contraction, and leftward shift of the interventricular septum due to right ventricular pressure load can be accurately measured. Such considerations were not accounted for in previous reports that provided data on wall motion of the bilateral ventricle.

To produce acute pulmonary embolism, a suspension of lycopodium spores in physiological saline was repeatedly infused 11 ± 6 times (mean $\pm$ SD) with an interval of about 5 min. This method allows stepwise induction of pulmonary hypertension by decreasing the pulmonary vascular bed functionally and mechanically.¹⁹⁻²²

In shock due to pulmonary embolism,

when RVSP reached a maximum value (62.8 ± 1.6 mmHg) (max-PH), LVSP was relatively well maintained (99.6 ± 1.8 mmHg). At the max-PH, though end-diastolic pressure was similar in the right and left ventricles, no reversion occurred. Morphologically, in end-diastole, an increase in RVD and a decrease in LVD were observed, and despite the leftward shift of the interventricular septum, the anterior and posterior walls, septum, and free wall of the left ventricle still moved centripetally.

The point of time at which LVSP decreased following repeated embolization to about 70 mmHg, CO to about 46% of the control value, and RVSP to about 50 mmHg after max-PH with an RVSP/LVSP of about 0.7 was chosen as the S-PH. The values at this point (S-PH) were similar to those found in shock due to pulmonary embolism, as defined by Molloy et al⁴ and Ducas et al²³ who showed the effectiveness of norepinephrine on hemodynamics. These values are also comparable to those given by Vlahakes et al²⁴ who suggested the importance of coronary perfusion. Morphologically, the leftward

shift of the interventricular septum became more severe, and LVD was not shortened in systole, but rather increased in some animals. After acute right ventricular loading, shortening of the left ventricular anterior-posterior diameter in systole was maintained, but systolic shortening of the interventricular septum-left ventricular free wall diameter was markedly limited, also causing severe left heart dysfunction.

At S-PH, at which point cardiac function was extremely impaired, the effects of ISO and NE administration and occlusion of the thoracic descending aorta were compared.

At S-PH, ISO, NE, and AO transiently elevated LVSP to the control value. HR increased most markedly with ISO but did not change following AO. CO increased after each treatment but only slightly after ISO. Stroke volume was increased by both NE administration and AO but decreased following ISO administration. In the right ventricle, RVSP was higher following NE administration than following ISO administration and was an intermediate value following AO.

ISO is considered to have more marked effects on myocardial contractility than NE. On the pulmonary vessels themselves, ISO has been reported to have dilating effects but NE has been shown to have constricting effects.^{5,25} AO has no such direct pharmacological effects as shown by Spotnitz et al.

In acute pulmonary embolism, ISO has been considered to be useful in terms of improvement of myocardial contractility and vasodilation and NE to be less useful because it increases right ventricular afterload. However, Ducas et al²⁶ recently evaluated the pressure-flow relationship in the pulmonary vessels in dogs with experimental pulmonary embolism and observed a decrease in pulmonary vascular resistance following ISO administration but no effects of NE on the tone of the pulmonary vessels. In our study, RVSP was the highest with NE followed in order by AO and ISO. Through these results do not directly support those of Ducas, the difference between NE and AO was small, suggesting that the effects of NE on pulmonary vascular contractility are small.

A comparison of LVEDP and RVEDP revealed an increase in LVEDP from about 6

to 10 mmHg, a decrease in RVEDP from about 16 to 12 mmHg, and a resultant decrease in the difference between the ventricles of about -10 to -2 mmHg following NE administration and AO. However, after the ISO administration, LVEDP decreased from about 6 to 4 mmHg and RVEDP from about 16 to 11 mmHg, decreasing the difference between the ventricles from about -10 to -7 mmHg. The apparent increase in CO was observed after the NE administration and AO suggests improvement in left ventricular filling due to improved right ventricular contractility. However, after the ISO administration, despite its enhancement of myocardial contractility, the increase in CO was slight, and HR increased. These findings suggest that impaired left ventricular filling was associated with decreased venous return to the right ventricle which was due to dilatation of peripheral vessels.

The leftward shift of the interventricular septum that developed in shock due to pulmonary embolism did not improve in diastole after the ISO administration but improved after either NE administration or AO. In systole, it also improved with NE or AO, resulting in the restoration of cooperative movement of LVAP and LVD. These changes corresponded to the above changes in the ventricular pressures. Our findings are consistent with the reports that the location of the interventricular septum during right ventricular loading can be explained by the difference in end-diastolic pressure between the ventricles.²⁷⁻²⁹

Direct enhancement of myocardial contractility and improvement of right ventricular coronary perfusion due to increased blood pressure have been suggested as mechanisms of improvement and maintenance of cardiac function by NE.^{4,30} Ducas et al, in an experiment using NE and methoxamine, reported that not only restoration in coronary perfusion pressure but also positive inotropic action is needed to improve right heart failure due to acute loading.²³ On the other hand, the similarity of NE to AO suggests that the restoration in coronary perfusion pressure is essentially important.

Vlahakes et al²⁴ produced acute right ventricular hypertension by pulmonary artery occlusion and measured blood flow and reactive hyperemia in the right coronary artery

and measured myocardial creatine phosphate. They observed, in right heart failure, a decrease in right coronary blood flow to 94% of the control value, disappearance of reactive hyperemia, and a decrease in right ventricular myocardial creatine phosphate to 45% of the control value. However, with increases in aortic pressure following phenylephrine administration, myocardial creatine phosphate recovered to 90% of the control value. Their findings suggest the importance of the restoration of coronary perfusion on myocardial ischemia due to acute right ventricular loading.

When RVSP is high, right coronary artery blood flow as with left coronary artery blood flow depends, to a larger degree, on diastole. Even though left ventricular systolic pressure increases by ISO administration, diastolic aortic pressure decreases because of the drug's effects. This decrease together with the shortening of diastole may aggravate coronary perfusion. In addition, tachycardia increases myocardial oxygen demand. As a result, there is high possibility that ISO accelerates cardiac ischemia.

Therefore, in the treatment of shock due to acute pulmonary embolism, restoration of systemic pressure, which is required for the maintenance of coronary perfusion, may be of primary importance.

Molloy et al evaluated the usefulness of ISO and NE on acute pulmonary hypertension in dogs with moderate right ventricular afterload and observed the effects of the reduction of the right ventricular afterload by ISO.¹⁵ There is also a report of the clinical use of ISO in acute respiratory failure.²⁵ When right ventricular afterload is not so severe, and blood pressure is not so low, ISO might be more effective than NE.

However, compared with the experiment by Molloy,¹⁵ we induced very severe pulmonary hypertension. In such severe shock, even though ISO reduced right ventricular afterload, decreased systemic blood pressure and tachycardia may have further aggravated coronary perfusion, resulting in a depressed cardiac contraction. On the other hand, NE increased coronary perfusion pressure as with AO, enhancing cardiac contraction.

Our results suggest that NE is superior to ISO for the improvement of hemodynamics in severe shock due to pulmonary embolism.

In addition, the ultrasonic method confirmed that NE improves not only the hemodynamics but also the leftward shift of the interventricular septum and cooperative contraction. In the future, under similar conditions, further detailed studies are needed on coronary blood flow and myocardial metabolism.

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