

## Impairment of coronary flow reserve and left ventricular function in the brain-dead canine heart

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### Abstract

**Objective:** The mechanisms of cardiac dysfunction after brain death, which are thought to be mainly associated with massive catecholamine release, have not been fully elucidated, especially with respect to the coronary circulation. The aim of this study was to investigate the changes in function of the coronary artery and its contribution to hemodynamic deterioration in a canine brain death model. **Methods:** Brain death was induced by rapid inflation of a subdurally placed balloon catheter. Hemodynamic measurements including assessment of left ventricular contractility using pressure–volume relations and biochemical analyses of blood samples were performed in seven dogs. Coronary flow reserve in the same brain death model was assessed by changes in coronary flow and resistance induced by administering a vasodilator directly into the coronary artery in another eight dogs. **Results:** A hyperdynamic response was transiently observed after induction of brain death, followed by decreases in arterial pressure, cardiac output, and coronary blood flow. Parameters of left ventricular contractility as measured by pressure–volume relations had significantly deteriorated by 60 min after brain death. Percent changes in coronary flow by administration of acetylcholine and sodium nitroprusside were 272 and 209%, respectively, before brain death; these were decreased to 178 and 145% at 30 min after brain death, and to 192 and 153% at 60 min. Coronary resistance ratios were also significantly increased at 30 and 60 min after brain death. **Conclusions:** Impairment of coronary flow reserve was found in the brain-dead canine heart. This impaired coronary circulation may constitute a disadvantage of prevention and recovery of cardiac dysfunction after induction of brain death.

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**Keywords:** Brain death; Coronary flow reserve; Heart failure; Transplantation

### 1. Introduction

Heart transplantation is the most reliable treatment for end-stage heart disease at present. Although surgical techniques, organ preservation, and immunosuppressive

treatments have been progressively advanced, primary graft failure is the most common cause of early mortality. In fact, about 20% of all recipient deaths after transplantation are due to non-specific graft failure that bears no relation to acute rejection or infection [1]. This implies that other mechanisms that can cause cardiac dysfunction should be considered. Some studies have demonstrated hemodynamic deterioration after brain death [2–9] and possible etiologies have been discussed, for example, catecholamine cardiotoxicity [2,3,6], imbalance between myocardial oxygen demand and supply [8,9], and hormone depression [7]. Although the exact mechanisms of cardiac dysfunction after induction of brain death are still unclear, it is suggested that massive catecholamine release after brain death plays an important role in hemodynamic deterioration [2,3,5–7].

Meanwhile, Galinanes and Hearse [10] have reported

**Abbreviations:** Ach, acetylcholine; AoF, aortic flow; AoP, aortic pressure; CBF, coronary blood flow; CVP, central venous pressure;  $dE/dt_{max}$ , slope of  $dP/dt_{max}-V_{ed}$  relation;  $dP/dt_{max}-V_{ed}$ , maximum first derivative of LV pressure versus end diastolic volume; ECG, electrocardiogram;  $E_{es}$ , slope of  $P_{es}-V_{es}$  relation; LA, left atrium; LAD, left anterior descending artery; LAP, left atrial pressure; LV, left ventricle; LVP, left ventricular pressure; mAoP, mean aortic pressure;  $M_{sw}$ , slope of  $SW-V_{ed}$  relation;  $P_{es}-V_{es}$ , end-systolic pressure–volume; SNP, sodium nitroprusside; SvO<sub>2</sub>, venous oxygen saturation;  $SW-V_{ed}$ , stroke work–end diastolic volume.

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that humoral and blood-borne factors may have a less important effect on cardiac function. Nevertheless, the mechanism of cardiac dysfunction by induction of brain death seems sophisticated and cannot be completely explained by catecholamines. Recently, the importance of coronary circulation to cardiac function after brain death has been pointed out. Szabo et al. [11] indicated that severe impairment of coronary flow might decrease the contractility of the heart after brain death, despite the absence of myocardial ischemia; the contribution of coronary circulation to cardiac dysfunction, however, could not be fully elucidated.

In the present study, we examined the changes in hemodynamics and cardiac function, as well as the responses of the coronary arteries, to vasodilators in a canine brain death model, in order to discuss the relationship between changes in coronary flow reserve and hemodynamic deterioration after brain death.

## 2. Materials and methods

### 2.1. Animal care

Twenty-two adult mongrel dogs weighing 14–24 kg were used in the present experiment, which was reviewed by the Ethics Committee on Animal Experiments in the Faculty of Medicine, Kyushu University, and was carried out under the control of the Guidelines for Animal experimentation in the Faculty of Medicine, Kyushu University and in accordance with The Law (No. 105) and Notification (No. 6) of the Japanese Government.

### 2.2. Induction of brain death

Under general anesthesia, brain death was induced by acute rise in intracranial pressure. A burr hole was drilled in the right front parietal region. A 16 Fr Foley catheter was placed in the subdural space and the balloon was rapidly inflated with normal saline (25 ml). Brain death was determined by the loss of corneal and pupillary reflexes, and the loss of respiration after cessation of anesthesia. This method for induction of brain death has been employed in previous reports [2,3,5–11,17,18].

### 2.3. Anesthesia and general preparation

The dogs were anesthetized with sodium thiamirial at a dose of 25 mg/kg intravenously (Isozol, Wellfide, Osaka, Japan). After endotracheal intubation, the dogs were artificially ventilated with 100% oxygen. The minute volume of ventilation was adjusted to maintain an arterial partial carbon dioxide pressure between 35 and 45 mmHg. Pancronium bromide (Masculax, N.V. Organon, Oss, The Netherlands) was intravenously administered at a dose of 0.1 mg/kg for muscle relaxation. Anesthesia was

maintained with inhaled isoflurane (Forane, Abbott, North Chicago, Illinois). A double-lumen catheter was inserted via the femoral vein for intravenous infusion and monitoring of central venous pressure (CVP). CVP was maintained at around 8 mmHg by administration of saline as necessary. An arterial catheter was inserted into the femoral artery to monitor arterial pressure (AoP) and to take blood samples for the analysis of blood gas and electrolytes. According to the values of calcium, bicarbonate, and base excess, substitution included administration of calcium chloride and sodium bicarbonate (8.4%).

### 2.4. Protocol 1: measurement of hemodynamics and left ventricle function

Fourteen adult mongrel dogs were used for protocol 1. After routine preparation, a median sternotomy and longitudinal pericardiotomy was performed to expose the heart. A catheter was inserted into the left atrium (LA) to measure LA pressure (LAP). A 10 Fr coronary sinus cannula was inserted for measurement of plasma lactate levels and oxygen content by blood sampling. A calibrated micro-manometer tipped catheter (Millar Mikro-Tip, Millar Instruments, Inc., Houston, TX, USA) was inserted into the left ventricle (LV) to measure left ventricular pressure (LVP). To measure the LV volume, a 7 Fr 12-electrode conductance catheter (Sentron B.V., Roden, The Netherlands) was inserted into the LV through the apex. The catheter was attached to a signal generator/processor (Sigma 5, Leycom, Leiden, The Netherlands). A 14-mm ultrasonic flow probe connected to a flowmeter (model T106, Transonic Systems, Inc., New York, NY) was positioned around the ascending aorta for the measurement of aortic flow (AoF), to calibrate the volume signal of the conductance catheter, as well as for continuous monitoring. Also, a 2-mm ultrasonic flow probe connected to another flowmeter (model T208, Transonic Systems, Inc.) was positioned around the left circumflex coronary artery for the measurement of coronary blood flow (CBF). The parallel conductance volume was calculated by transiently altering blood conductivity by the injection of hyper saline solution (10 ml of 10% NaCl) [12].

#### 2.4.1. Experimental design

The electrocardiogram (ECG), AoP, CVP, LAP, AoF, and CBF were continuously monitored. After 10 min of equilibrium since the final preparation, control measurements of LV contractility, using pressure–volume relations and blood sampling, were performed. Then the dogs were divided into two groups. Seven animals with a sham operation served as the sham group. The other seven animals were subjected to brain death. Blood sampling from the femoral artery and coronary sinus, for measuring oxygen saturation and plasma lactate concentration, was performed at 1, 5, 30, and 60 min after induction of brain death. At the last

time point, measurements of LV contractility using pressure–volume relations were also performed.

#### 2.4.2. Data analysis of LV function

Multiple LVP–volume loops were obtained during transient preload reduction by IVC occlusion. Computer algorithms using a C-language type program developed in our laboratory with an Intel 486-based personal computer (Vision, IBM Japan, Tokyo, Japan) analyzed the digitized data. LV contractility was evaluated by the end-systolic pressure–volume ( $P_{es}$ – $V_{es}$ ) relation, the stroke work versus end diastolic volume ( $SW$ – $V_{ed}$ ) relation, and the maximum first derivative of LVP versus end diastolic volume ( $dP/dt_{max}$ – $V_{ed}$ ) relation. The  $P_{es}$ – $V_{es}$  relation was fitted by linear regression to obtain the slope ( $E_{es}$ ) and volume intercept ( $V_{0,es}$ ) and the volume associated with  $P_{es}$  of 100 mmHg ( $V_{100,es}$ ) was calculated.  $SW$  was plotted against  $V_{ed}$  to obtain the slope ( $M_{sw}$ ) and the volume intercept ( $V_{0,sw}$ ) of the  $SW$ – $V_{ed}$  relation. The end diastolic point was defined as the point of the rapid upstroke of the first derivative of LVP ( $dP/dt$ ). The position of the  $SW$ – $V_{ed}$  relation in the operating range was calculated by determining the  $V_{ed}$  associated with a  $SW$  of 500 mmHg ml ( $V_{500,sw}$ ). The slope ( $dE/dt_{max}$ ) and volume intercept ( $V_{0,dP/dt}$ ) of the  $dP/dt_{max}$ – $V_{ed}$  relation were obtained in the same way, and the  $V_{ed}$  associated with a  $dP/dt_{max}$  of 1000 mmHg/s ( $V_{1000,dP/dt}$ ) was calculated [13]. When we evaluate ventricular function using the pressure–volume relations, the position of the relations is also important.  $V_{100,es}$ ,  $V_{500,sw}$ , and  $V_{1000,dP/dt}$  were the parameters of the position of the relations. When the relations shifted to the right, it indicated the deterioration of LV function.

#### 2.5. Protocol 2: measurement of coronary reserve

The other eight mongrel dogs were anesthetized in the same manner as above. After routine preparation, a left thoracotomy was performed in the fourth intercostal space. A 2-mm ultrasonic flow probe was placed at the mid-portion of the left anterior descending coronary artery (LAD) to measure CBF, as previously described [14,22]. The maximum increases of CBF in response to acetylcholine (Ach) and sodium nitroprusside (SNP) were used for analysis; a heparin-filled tube (3 Fr size) was inserted into the first or second diagonal branch of the LAD for infusion of these agents [14,21]. Endothelium-dependent (Ach) and endothelium-independent (SNP) coronary relaxation were measured before brain death and at 30 and 60 min afterward. The CBF was recorded from the beginning of infusion until its return to the baseline. Ach (3  $\mu$ g) and SNP (100  $\mu$ g) were infused for 60 s. The coronary flow reserve

was calculated as follows:

Percent change of CBF

$$= (\text{maximum flow} - \text{baseline flow}) / \text{baseline flow} \times 100 + 100 (\%)$$

The coronary resistance ratio, which has minimal dependence on perfusion pressure [15], was calculated as follows [16]:

Coronary resistance ratio

$$= \text{coronary resistance at maximum flow} / \text{coronary resistance at baseline}$$

#### 2.6. Statistical analysis

Data were presented as mean  $\pm$  standard deviation. The Student's paired  $t$  test was used for the variables determined once during the experiment to examine the difference between two groups. Intragroup comparisons were achieved using one-way analysis of variance (ANOVA) followed by Fisher's PLSD test. Probability values less than 0.05 were considered statistically significant. Statistical analysis was performed using the StatView 5.0 software package (SAS Institute, Cary, NC).

### 3. Results

#### 3.1. Hemodynamic changes

In the sham group ( $n = 7$ ), no significant hemodynamic change was observed throughout the protocol (Table 1). In the brain death group, a transient hyperdynamic response was observed immediately after the induction of brain death (Table 1). Specifically, systolic AoP (sAoP), mAoP, AoF, CBF, and heart rate (HR) were all significantly increased at 1 and 5 min after brain death. This initial hyperdynamic response persisted for about 15 min. Hemodynamic variables had decreased to the control values by 30 min after brain death. At 60 min after brain death, sAoP and mAoP showed significant decreases ( $p < 0.01$ ), compared with the control values. AoF and CBF were also decreased at 60 min after brain death, but these changes were not statistically significant (Table 1).

#### 3.2. LV function

Parameters of left ventricular function are shown in Table 2. Indices of left ventricular function, namely  $E_{es}$ ,  $M_{sw}$ , and  $dE/dt_{max}$  at 60 min after brain death were all significantly decreased in comparison with control values.

Table 1  
Change in parameters of hemodynamics

	Control	1 min	5 min	30 min	60 min
<b>Sham group</b>					
sAoP (mmHg)	127.0 ± 14.7	125.1 ± 27.6	135.0 ± 22.7	135.9 ± 11.4	132.0 ± 19.3
mAoP (mmHg)	99.7 ± 13.1	100.3 ± 23.7	109.2 ± 21.3	109.8 ± 17.0	109.2 ± 18.9
AoF (l/min)	1.2 ± 0.4	0.89 ± 0.2	0.91 ± 0.2	0.91 ± 0.3	0.89 ± 0.2
CBF (ml/min)	20.9 ± 5.7	21.6 ± 9.2	21.5 ± 7.9	21.7 ± 10.1	22.4 ± 9.1
HR (bpm)	149.5 ± 19.8	141.4 ± 13.0	142.9 ± 16.9	143.0 ± 17.7	139.5 ± 21.3
<b>Brain death group</b>					
sAoP (mmHg)	134.8 ± 16.3	323.2 ± 49.3*	204.0 ± 29.3*	88.9 ± 23.2**	68.1 ± 16.9*
mAoP (mmHg)	100.8 ± 14.4	233.5 ± 53.1*	151.6 ± 45.8*	57.4 ± 8.4*	56.4 ± 9.3*
AoF (l/min)	1.2 ± 0.3	2.5 ± 1.3*	2.2 ± 0.8**	1.0 ± 0.5	0.63 ± 0.3
CBF (ml/min)	17.1 ± 2.2	192.5 ± 62.6*	130.0 ± 57.2*	16.2 ± 3.2	10.9 ± 1.5
HR (bpm)	154.8 ± 14.0	226.3 ± 24.4*	202.2 ± 23.8*	165.4 ± 17.8	140.9 ± 18.2

\* $p < 0.01$  versus control; \*\* $p < 0.05$  versus control.

sAoP, systolic arterial pressure; mAoP, mean arterial pressure; AoF, aortic flow; CBF, coronary blood flow; HR, heart rate.

Thus, the three relations were significantly shifted to the right after brain death, manifested by the differences in  $V_{100,es}$ ,  $V_{500,SW}$ , and  $V_{1000,dP/dt}$ .

### 3.3. Venous oxygen saturation and lactate

The measured values of oxygen saturation in the coronary sinus ( $SvO_2$ ), serum lactate concentration, and its veno-arterial difference (V-A lactate) before induction of brain death and at 1, 5, 30, and 60 min afterward are shown

Table 2  
The effects of brain death on LV function

$P_{es}-V_{es}$ relation		
	$E_{es}$ (mmHg/ml)	$V_{100,es}$ (ml)
Control	8.4 ± 2.2	12.0 ± 5.1
Brain death	4.1 ± 0.8	18.5 ± 6.3
<i>p</i> value	0.0009	0.0016
$SW-V_{ed}$ relation		
	$M_{sw}$ (mmHg)	$V_{500,SW}$ (ml)
Control	77.0 ± 7.5	15.1 ± 4.5
Brain death	34.4 ± 16.1	21.6 ± 9.5
<i>p</i> value	0.0014	0.0050
$dP/dt_{max}-V_{ed}$ relation		
	$dE/dt_{max}$ (mmHg/s ml)	$V_{1000,dP/dt}$ (ml)
Control	64.1 ± 16.1	7.5 ± 7.5
Brain death	30.7 ± 12.5	24.2 ± 16.4
<i>p</i> value	0.0034	0.0010

$P_{es}$ , left ventricular end-systolic pressure;  $V_{es}$ , end-systolic volume;  $E_{es}$ , slope of  $P_{es}-V_{es}$  relation;  $V_{100,es}$ ,  $V_{es}$  associated with  $P_{es}$  of 100 mmHg; SW, left ventricular stroke work;  $V_{ed}$ , end diastolic volume;  $M_{sw}$ , slope of  $SW-V_{ed}$  relation;  $V_{500,SW}$ ,  $V_{ed}$  associated with stroke work of 500 ml mmHg;  $dP/dt_{max}$ , maximum rate of change of left ventricular pressure;  $dE/dt_{max}$ , slope of  $dP/dt_{max}-V_{ed}$  relation;  $V_{1000,dP/dt}$ ,  $V_{ed}$  associated with  $dP/dt_{max}$  of 1000 mmHg/s.  $E_{es}$ ,  $M_{sw}$ , and  $dE/dt_{max}$  are significantly decreased compared with baseline value. Three relations are shifted toward the right.

in Table 3.  $SvO_2$  had increased at 1 min after brain death and had significantly decreased at 30 and 60 min. Although the plasma lactate concentrations as sampled from the femoral artery and coronary sinus increased gradually, no significant change in V-A lactate (i.e. myocardial lactate extraction) was observed during this experiment.

### 3.4. Coronary flow reserve

Percent changes in coronary flow and coronary resistance ratios induced by Ach and SNP are illustrated in Figs. 1 and 2. Percent changes in coronary flow by administration of Ach were significantly reduced from  $272 \pm 42\%$  before brain death to  $178 \pm 50\%$  and  $192 \pm 33\%$  at 30 and 60 min after brain death, respectively ( $p = 0.0004$ ). The same changes in coronary flow were obtained when SNP was administered. Coronary resistance ratios were significantly increased by administration of Ach from  $0.37 \pm 0.07$  before brain death to  $0.61 \pm 0.13$  and  $0.54 \pm 0.09$  at 30 and

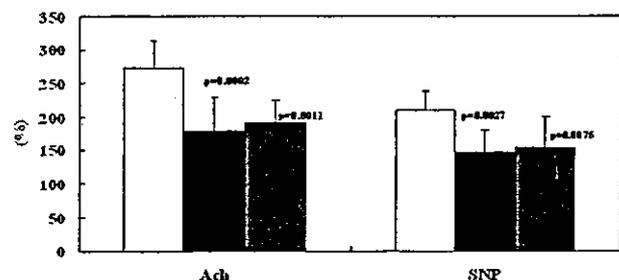


Fig. 1. Changes in percent increase of CBF by administration of Ach and SNP. Ach (3  $\mu$ g) and SNP (100  $\mu$ g) were directly injected into the coronary artery for 60 s. Percent change in CBF was calculated as described in Section 2. The values of percent increase in CBF at 30 min (black bar) and 60 min (gray bar) are compared with the control value (white bar). Both the Ach ( $p = 0.0004$ ) and SNP ( $p = 0.0052$ ) induced increases in CBF were significantly impaired at 30 and 60 min after brain death as determined by one-way ANOVA. The *p* values given were obtained by Fisher's PLSD test.

Table 3  
Changes in SvO<sub>2</sub> and concentration of lactate

	Control	1 min	5 min	30 min	60 min
SvO <sub>2</sub> (%)	80.5 ± 4.9	87.2 ± 3.4	85.2 ± 7.3	69.3 ± 10.7*	67.4 ± 11.0**
A lactate (mg/dl)	31.3 ± 12.6	38.0 ± 17.5	38.7 ± 16.1	50.8 ± 29.5	46.7 ± 26.7
V lactate (mg/dl)	30.7 ± 11.1	36.4 ± 13.7	35.9 ± 17.9	47.1 ± 24.4	42.8 ± 22.1
V-A lactate	-2.0 ± 2.9	-1.6 ± 5.0	-2.8 ± 5.7	-3.7 ± 11.6	-3.1 ± 5.8

\**p* < 0.05 versus control; \*\**p* < 0.01 versus control.

SvO<sub>2</sub>, venous oxygen saturation in coronary sinus; A lactate and V lactate, plasma lactate level femoral artery and coronary sinus; V-A lactate, veno-arterial difference of plasma lactate level.

60 min after brain death, respectively (*p* = 0.0004). Again, the exact same results for the coronary resistance ratios were obtained when SNP was administered.

#### 4. Discussion

It is known that induction of brain death can cause hemodynamic deterioration. Some possible mechanisms of cardiac dysfunction have been discussed in previous studies [2–9], in which a catecholamine storm related to the Cushing reaction was thought to be important [3,6]. Shilvalkar et al. [17] reported that this extreme catecholamine release is associated with histological myocardial damage, which could be due to myocardial toxicity of catecholamine. Novitzky et al. [3] reported that increased endogenous catecholamine release from sympathetic nerve endings induces LV dysfunction, which possibly results in increased calcium uptake by the myocardial cell. These studies indicate that a massive release of catecholamines plays an important role in LV dysfunction after brain death.

The importance of coronary artery function on hemodynamic deterioration after brain death has been recently discussed. Szabo et al. [11] reported that severe impairment

of CBF might contribute to a decreased contractility after brain death that could be reversed by modulation of coronary perfusion pressure. Seguin et al. [18] reported that myocardial ischemia induced by a limited increase in CBF, which might be caused by norepinephrine from cardiac sympathetic nerve endings, was the important mechanism of hemodynamic deterioration after brain death. However, this is yet to be completely clarified.

In the present study, impairment of hemodynamics and LV function as measured by pressure–volume relations was clearly demonstrated at 60 min after brain death, as previously reported [6,8,9]. We also found that coronary reserve was already impaired at 30 min after induction of brain death. Because coronary reserve is known to relate to coronary microcirculation [19], LV dysfunction after brain death may have some relation to this impairment of coronary microcirculation.

Several studies [8,9,18] have suggested that a possible mechanism of LV dysfunction after brain death is an imbalance between myocardial oxygen demand and supply during the transient hyperdynamic state. Delophont et al. [9] found an increase in AoP—but only a limited increase in CBF—resulting in a significant increase in interstitial adenosine production in the hyperdynamic state in a brain-dead pig model. In contrast, we observed the maximum increase in CBF and AoP at 1 min after induction of brain death. In addition, we found increased SvO<sub>2</sub> from the coronary sinus but no decrease during the hyperdynamic state. This difference seems to be due to the animal species or the experimental circumstances. On the other hand, in the present study, SvO<sub>2</sub> was significantly decreased to 69.3% at 30 min and 67.4% at 60 min after brain death, despite lack of evident myocardial lactate production. Seguin et al. [18] used a more sensitive microdialysis method for the measurement of interstitial lactate and adenosine level, to detect imbalance between myocardial oxygen demand and supply. Such an imbalance, at the level of the coronary microcirculation, might occur even during the hyperdynamic state, although we could find no evidence of global myocardial ischemia. The impairment of coronary microcirculation might induce or promote a myocardial oxygen imbalance, resulting in the impairment of hemodynamics and cardiac function.

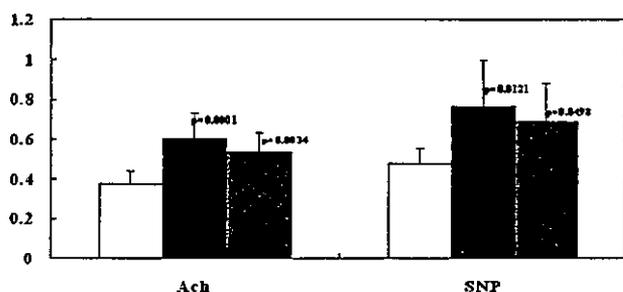


Fig. 2. Changes in coronary resistance ratio in response to Ach and SNP. Ach (3 µg) and SNP (100 µg) were directly injected into the coronary artery for 60 s. Coronary resistance ratio was calculated as described in Section 2. The values of percent increase in CBF at 30 min (black bar) and 60 min (gray bar) were compared with the control value (white bar). Coronary resistance ratio was significantly increased at 30 and 60 min after brain death by both Ach (*p* = 0.0004) and SNP (*p* = 0.0312) as determined by one-way ANOVA. The *p* values given were obtained by Fisher's PLSD test.

Reduced coronary reserve is known to be caused by disturbance of the coronary microcirculation, which is based on impaired blood flow in the small (<200  $\mu\text{m}$ ) intramural arteriolar resistance vessels or the coronary capillary system, or both [19]. Chilian et al. [20] reported that high dose norepinephrine and high frequency stellate stimulation produced vasoconstriction in coronary vessels greater than 100  $\mu\text{m}$  in diameter, although vasodilation was observed in arterioles less than 100  $\mu\text{m}$  in diameter. Moreover, the impairment of coronary reserve was also observed at 60 min after brain death, when catecholamine concentrations had already normalized (data not shown). This implies that impairment of coronary microcirculation cannot be fully explained by catecholamines alone.

The coronary flow reserve, as obtained by direct injection of Ach and SNP into a coronary artery, was impaired at 30 and 60 min after brain death. Coronary flow reserve is known to be influenced by blood pressure, HR, and preload [15]. HR was not significantly changed between the control state and 30 or 60 min after brain death, while preload was also unchanged because LAP and CVP were unchanged (data not shown), even though mAoP values were significantly different at these points. Therefore, we also examined the coronary resistance ratio, which is known to have minimum dependence on perfusion pressure [15]; we found significant increases in coronary resistance ratios at 30 and 60 min after brain death.

We observed only for 60 min after brain death, because hemodynamic data did not change after 60 min in previous reports [6,8,9,18]. Reduced coronary flow reserve was also reported as the predictors of performance in the chronic phase after heart transplantation [22,23]. Besides, endothelium-independent microvascular dysfunction was reported to have prognostic importance for deterioration of left ventricular function in cardiac transplant recipients [23]. In the present study, we could observe impaired coronary flow reserve only in the early phase after brain death, but impairment of coronary reserve may have some adverse effects on functional recovery of transplanted heart in the chronic phase.

In conclusion, LV dysfunction and impairment of coronary reserve were observed in a brain-dead canine heart. Our data suggest that impairment of coronary reserve, which can imply impairment of coronary microcirculation, probably have some relation to hemodynamic deterioration and cardiac dysfunction after brain death.

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