EFFECTS OF EXTRACORPOREAL CIRCULATION ON CARDIAC PERFORMANCE AND CORONARY BLOOD FLOW (TOTAL AND REGIONAL)

A Study of Differences Arising from Pre-Existent Left Ventricular Load and Anoxic Arrest

ETSUO MONDORI

AS a result of post-mortem findings in patients dying from the low cardiac output syndrome (LOS)^{1,2} and experiments with animals,³ subendocardial ischemia and hemorrhagic necrosis have been indicated as one causative factor of LOS – a serious complication of open-heart surgery. On the other hand, Okada et al⁴, studying hemorrhagic shock, failed to demonstrate any correlation between decreased myocardial contractility and changes in the distribution of blood flow to the wall of the left ventricle and thus were unable to explain the decrease in contractility as being due to changes in the distribution of blood flow within the left ventricular wall.

In the present experiments, normal hearts were compared with hearts in which left ventricular hypertrophy had been induced experimentally. These two groups were further subgrouped (a total of 4 groups) on the basis of whether or not anoxic arrest for 40 mins. (by intermittent aortic cross clamping) was also performed. Each of these groups underwent 60 mins. of extracorporeal circulation (ECC) with cardiac performance being assessed before and after ECC. Regional blood flow was measured with $15 \pm 5 \mu$

diameter radioactive microspheres at three points in time: in groups not subjected to anoxic arrest, these were before ECC, after 60 mins. of ECC, and 60 mins. after the cessation of ECC; in groups subjected to anoxic arrest, these were before anoxic arrest, after declamping, and 60 mins. after the cessation of ECC. The total blood flow, the flow to each part of the heart, and, to study the correlation with cardiac performance, the flow to inner, middle, and outer layer of the left ventricle were all measured. The changes in cardiac performance of each group and the changes in total coronary blood flow, regional coronary blood flow, and the distribution of blood flow within the left ventricle were compared.

The object of this study is to determine the extent of correlation between changes in cardiac performance and changes in the distribution of blood flow in each experimental group.

METHOD

1) Experimental protocol.

Mongrel dogs weighing 7–12 kg were anesthetized with intravenous pentobarbital (25 mg/kg), panchronium bromide (0.3 mg/kg) injected intravenously and positive pressure breathing established through an intratracheal tube.

The left femoral artery and vein were exposed and catheter inserted for monitoring arterial and central venous pressure. An arterial catheter was connected to a transducer MPU-0.5-290 (SANEI

Key Words

Extracorporeal circulation
Anoxic aortic cross clamping
Experimentally hypertrophied cardiac muscle
Cardiac performance
Regional coronary blood flow
Radioactive microsphere

(Received on March 6, 1979; Accepted on November 26, 1979)

The 2nd Dept. of Surg., Okayama Univ. Med. Sch.

The outline of this paper was presented partially at the 30 Annual Meeting of the Japanese Association for Thoracic Surgery and partially the 43 Annual of Meeting the Japanese Circulation Society.

Fig.1. The courses of experiments.

Instrument Co.). Venous pressure was monitored by hydraulic pressure. A Swan-Gantz catheter was inserted in the pulmonary artery from the left external jugular vein for measuring cardiac output. A Millar microtip transducer was inserted in the left ventricle via the left carotid artery for monitoring left ventricular pressure (LVP), left ventricular enddiastolic pressure (LVEDP) and Vmax.

Immediately after the right chest was opened through the fourth intercostal space, the administered gas was changed to 100% oxygen. After longitudinal pericardiotomy, a vinyl tube was inserted through the left auricle for monitoring of left atrial pressure and for injecting the microspheres (MS) and the left atrial vent. This vinyl tube was connected to a transducer LPU-0.1-350 (SANEI Instrument Co.). All pressures except venous pressure were recorded on a polygraph No. 141-6 (SANEI Instrument Co.). Another vinyl tube was inserted through a purse string suture on the right atrial wall for sampling coronary sinus blood.

The extracorporeal circuit was constructed by inserting an arterial cannula into the right femoral artery and venous cannulae into the superior and the inferior venae cavae through the right atrium with gravity venous drainage. Hemodilution (20%) was achieved with Haemaccel and Ringer's solution. The pH of the priming solu-

tion was corrected with 7% sodium bicarbonate. A vent was inserted into the right ventricle through the right atrium. 9 inch Kay-Cross type disc oxygenator and a DeBakey type double roller pump were used. A Braun-Harrison type heat exchanger was set into the arterial line for maintaining body temperature at 36–37°C. The perfusion rate was 2.0 L/min/M² and the total time of ECC was 60 minutes.

The dogs were divided into the following four groups (Fig. 1).

Group I (9 dogs)

non-hypertrophied heart without anoxic arrest.

Group II (9 dogs)

non-hypertrophied heart with intermittent aortic cross clamping (5 mins. reperfusion inserted between two trials of 20 mins. anoxic arrest).

Group III (6 dogs)

hypertrophied heart without anoxic arrest.

Group IV (7 dogs)

hypertrophied heart with intermittent aortic cross clamping (same as in group II).

Hypertrophied hearts were created by stenosing the ascending aorta of young dogs weighing 1.5–3 kg with teflon tapes for 4–6 months. At the time of experiment, the pressure difference at the stenotic site was 23 mmHg (mean) in group III. The LV/RV weight ratio was 1.75–2.60

TABLE I BLOOD GAS ANALYSIS IN GROUP I

		Pre-ECC			ECC 5 min			ECC 30 min			ECC 60 min			Post-ECC		
<i>m</i> -AP (mmHg)		113.3	(9.3)	* ¹	90.8	(6.4)	* ¹	88.3	(3.8)	* ¹	86.1	(3.6)	* ¹	89.7	(7.8)	* ¹
PH	A	7.379	(0.039)	* ²	7.429	(0.025)		7.366	(0.021)		7.363	(0.024)		7.118	(0.023)	* ²
	V	7.323	(0.032)		7.359	(0.025)		7.320	(0.016)		7.306	(0.021)		7.096	(0.018)	
	CS	7.311	(0.034)		7.397	(0.029)		7.313	(0.026)		7.304	(0.018)		7.101	(0.021)	
PO ₂ (mmHg)	A	119.6	(28.3)	* ³	171.2	(40.7)		154.7	(26.9)		190.5	(16.3)		56.2	(5.0)	* ³
	V	38.7	(5.0)		49.2	(3.0)		48.7	(2.2)		46.6	(2.0)		34.7	(3.3)	
	CS	28.1	(3.5)		26.6	(2.2)		24.3	(2.1)		27.0	(2.8)		33.8	(1.6)	
PCO ₂ (mmHg)	A	31.7	(2.6)	* ⁴	27.9	(1.1)		28.2	(1.7)		28.8	(1.4)		52.9	(3.0)	* ⁴
	V	38.9	(2.0)		36.6	(1.6)		36.1	(1.7)		36.6	(1.3)		65.3	(3.8)	
	CS	43.8	(2.6)		36.6	(1.6)		38.4	(2.1)		41.3	(2.2)		60.9	(3.9)	
Hb (g/dl)		13.6	(0.7)		11.1	(0.4)		11.7	(0.3)		11.6	(0.5)		13.4	(0.6)	
A-CS O ₂ diff (vol%)		9.55	(1.19)	* ⁵	7.95	(0.66)		9.62	(0.81)		10.05	(0.65)		4.76	(0.58)	* ⁵
O ₂ consumption (ml/min/100g)		7.88	(1.45)	* ⁶	—			—			3.62	(0.42)	* ⁶	6.22	(0.62)	
CVP (cm H ₂ O)		5.2	(0.4)		10.6	(1.1)		11.8	(0.7)		12.0	(0.6)		11.1	(1.8)	

AP: arterial pressure A: arterial V: venous CS: coronary sinus mean (SE)

ECC: extracorporeal circulation

*¹ $P < 0.05$ *² $P < 0.001$ *³ $P < 0.001$ *⁴ $P < 0.001$ *⁵ $P < 0.001$ *⁶ $P < 0.06$ *⁷ $P < 0.01$

(mean 2.02 ± 0.26). In group IV, the mean pressure difference was 26 mmHg. The LV/RV weight ratio was 1.78–2.86 (mean 2.00 ± 0.14). In group I and II, the LV/RV weight ratio was 1.49 and 1.48. There was a significant difference ($p < 0.001$) between LV/RV weight ratio in group I and II and that in group III and IV.⁵

2) Measurements

a) Blood gas analysis and cardiac performance.

In group I and III, at the end of inserting catheter for monitoring pressures, the arterial, venous, and coronary sinus samples were collected and analyzed for pH, pO₂ and pCO₂ with a blood gas analyzer No. 165 (CORNING Co.). At the same time, arterial pressure, central venous pressure, heart rate, LAP, LVEDP, cardiac output by thermodilution, and Vmax by MASON's⁶ exploration method were measured. Left ventricular stroke work (LVSW) was calculated as follows, $LVSW = LVP \times SVI \times 1.36 \times 10^{-2}$ g-meters. Blood gases were analyzed at 5 mins., 30 mins., and 60 mins. of ECC. In group II and IV, controls were measured at the same time as in group I and III, and blood gases were

analyzed at 5 mins., 30 mins. (after a 20 mins. interval of anoxic arrest and 5 mins. of reperfusion), and 60 mins. of ECC.

Sixty mins. after the end of ECC, cardiac performance was measured and blood gases were analyzed in all groups.

b) Total and regional coronary blood flow Fig. 1)

According to the method which Rudolph and Heymann⁷ used, total and regional coronary blood flow was measured using $15 \pm 5 \mu$ diameter radioactive microspheres (MS) which were labeled with each of ¹²⁵I, ⁵¹Cr and ⁸⁵Sr.

In group I and III, at the three times of (1) before ECC, (2) after 60 mins. of ECC, and (3) 60 mins. after ECC, MS were injected into the arterial line (during ECC) or into the left atrium. In group II and IV, at the three times of (1) after 5 mins. of ECC, (2) after 60 mins. of ECC and (3) 60 mins. after ECC, MS were injected in the same way as for group I and III. MS were injected throughout ECC at the single time of after 60 mins. of ECC in group I and III because there was almost no change in the total coronary blood flow during ECC in Senoo's

TABLE II BLOOD GAS ANALYSIS IN GROUP II

		Pre-ECC			ECC 5 min			ECC 30 min			ECC 60 min			Post-ECC		
<i>m</i> -AP (mmHg)		108.0	(5.1)	)* ¹	77.2	(5.5)	)* ¹	75.2	(5.3)	)* ¹	80.6	(5.9)	)* ¹	76.7	(6.0)	)* ¹
PH	A	7.314	(0.027)	)* ²	7.443	(0.024)		7.328	(0.023)		7.324	(0.013)		7.176	(0.029)	)* ²
	V	7.273	(0.026)		7.381	(0.028)		7.267	(0.026)		7.275	(0.013)		7.120	(0.025)	
	CS	7.269	(0.027)		7.397	(0.031)		7.299	(0.023)		7.293	(0.010)		7.164	(0.027)	
PO ₂ (mmHg)	A	186.3	(25.5)	)* ³	125.3	(23.3)		166.9	(30.3)		143.0	(23.1)		65.3	(7.2)	)* ³
	V	51.3	(5.8)		44.21	(2.9)		45.8	(2.0)		46.5	(2.3)		38.6	(3.9)	
	CS	40.9	(5.9)		23.4	(3.2)		45.9	(3.5)		30.9	(6.0)		37.3	(6.1)	
PCO ₂ (mmHg)	A	39.2	(2.2)	)* ⁴	31.5	(2.3)		30.7	(1.9)		35.3	(3.5)		50.5	(4.6)	)* ⁴
	V	45.4	(2.8)		40.7	(2.3)		41.0	(3.2)		41.4	(3.7)		61.3	(4.4)	
	CS	47.2	(3.0)		41.3	(2.7)		38.8	(2.7)		41.6	(2.6)		56.3	(3.8)	
Hb (g/dl)		13.6	(0.7)		10.6	(0.6)		10.2	(0.6)		10.2	(0.8)		11.9	(0.7)	
A-CS O ₂ diff. (vol %)		7.58	(1.22)	)* ⁵	8.32	(1.09)		3.56	(0.60)		5.28	(1.17)		4.60	(0.79)	)* ⁵
O ₂ consumption (ml/min/100g)		—			3.20	(1.08)	)* ⁶	—			3.17	(0.45)		6.61	(0.98)	)* ⁶
CVP (cm H ₂ O)		4.6	(0.3)		8.9	(1.4)		8.9	(0.9)		9.3	(1.0)		10.4	(1.1)	

AP: arterial pressure A: arterial V: venous CS: coronary sinus mean (SE)

ECC: extracorporeal circulation

*¹ $P < 0.002$ *² $P < 0.002$ *³ $P < 0.008$ *⁴ $P < 0.03$ *⁵ $P < 0.05$ *⁶ $P < 0.05$ *⁷ $P < 0.0004$

report.⁸ In group II and IV, to study the effect of anoxic arrest on total and regional coronary blood flow, MS were injected after 5 mins. of ECC and after 60 mins. of ECC and the blood flow was measured.

At the end of each experiment, the heart was excised and divided into atria, septum, right ventricular free wall and left ventricular free wall. The left ventricular free wall was divided into three layers (inner, middle, and outer layer). The radioactivity for each nuclide in each region of interest was counted with a well scintillation detector connected to a universal gamma counter (TD-6 NIPPON WIRELESS Co.). At the time when injecting MS, a reference sample was collected from the catheter in the left femoral artery.

The blood flow in each region was calculated as follows.

Total coronary blood flow =

$$\frac{\text{Volume of reference sample (ml/min.)} \times \text{total count for whole heart (/100 g)}}{\text{count for reference sample}}$$

Regional blood flow =

$$\frac{\text{volume of reference sample (ml/min.)} \times \text{count for the region of interest (/100 g)}}{\text{count for reference sample}}$$

In measuring the blood flow by MS, adequate attention was paid to the problem of MS usage previously reported^{9,10}

RESULTS

1) Blood gas analysis and circulatory parameters (Table I, II, III, IV).

The mean blood pressure after ECC fell significantly in groups I ($p < 0.05$), II ($p < 0.0002$) and III ($p < 0.01$), but in group IV, the fall was only slight. The perfusion rate maintained at 2.0 L/min./M² in all groups. The mean blood pressure in group I and group II (Table I, II) was more than 75 mmHg and in group III and group IV (Table III, IV), more than 90 mmHg. In all groups, the arterial pH after ECC fell. This was significant in group I ($p < 0.001$) and group II ($p < 0.002$). The arterial pCO₂ also increased significantly after ECC in all groups except group III, the increase being the most marked in group

TABLE III BLOOD GAS ANALYSIS GROUP III

		Pre-ECC		ECC 5 min		ECC 30 min		ECC 60 min		Post-ECC	
<i>m-AP (mmHg)</i>		125.0	(11.3) ^{*1}	109.2	(5.2)	104.2	(7.0)	98.3	(8.0)	92.5	(5.4) ^{*1}
<i>PH</i>	<i>A</i>	7.327	(0.023)	7.451	(0.037)	7.386	(0.037)	7.314	(0.045)	7.277	(0.029)
	<i>V</i>	7.260	(0.019)	7.407	(0.031)	7.341	(0.031)	7.276	(0.048)	7.255	(0.037)
	<i>CS</i>	7.258	(0.021)	7.400	(0.025)	7.336	(0.040)	7.276	(0.052)	7.247	(0.031)
<i>PO₂</i> (mmHg)	<i>A</i>	299.6	(34.7) ^{*2}	370.0	(54.1)	256.1	(38.5)	287.9	(25.6)	64.8	(8.9) ^{*2}
	<i>V</i>	57.3	(6.0)	67.1	(7.3)	53.9	(3.7)	54.0	(1.7)	43.4	(2.4)
	<i>CS</i>	36.5	(7.2)	35.1	(3.2)	25.9	(1.2)	32.1	(6.4)	36.3	(3.7)
<i>PCO₂</i> (mmHg)	<i>A</i>	32.7	(1.4)	27.1	(0.5)	29.2	(1.4)	31.8	(2.5)	25.6	(2.1)
	<i>V</i>	37.1	(1.1)	31.0	(1.6)	34.8	(1.4)	34.1	(3.7)	37.8	(3.3)
	<i>CS</i>	42.8	(1.6)	31.4	(3.1)	37.9	(2.2)	39.6	(4.8)	42.5	(2.5)
<i>Hb (g/dl)</i>		13.0	(0.4)	10.7	(0.7)	10.3	(0.7)	10.0	(0.5)	11.0	(0.4)
<i>A-CS O₂ diff</i> (vol %)		9.61	(1.65) ^{*3}	4.38	(0.81)	6.42	(1.42)	6.40	(1.23)	4.11	(1.37) ^{*3}
<i>O₂ consumption</i> (ml/min/100g)		7.46	(2.20)	—		—		4.74	(1.17)	7.45	(2.32)
<i>CVP (cm H₂O)</i>		5.8	(0.9) ^{*4}	5.8	(1.3)	8.9	(1.5)	8.9	(1.4)	8.4	(0.4) ^{*4}

AP: arterial pressure *A*: arterial *V*: venous *CS*: coronary sinus mean (SE)

ECC: extracorporeal circulation

*1 $P < 0.01$ *2 $P < 0.002$ *3 $P < 0.05$ *4 $P < 0.05$

I ($p < 0.001$) and group II ($p < 0.03$). Although the arterial pO_2 after ECC was significantly ($p < 0.003$) higher in group IV than in the other groups, it was low in all groups and the conditions of lungs after ECC was in question.

The A-CS oxygen difference before ECC was significantly ($p < 0.05$) lower only in group IV. It showed a significant decrease after ECC in groups I ($p < 0.001$), II ($p < 0.05$), and III ($p < 0.05$) compared to before ECC. In group I, it did not change during ECC. In group II, it fell after anoxic arrest. In group III, it fell immediately after the beginning of ECC and increased gradually during ECC. In group IV, it tended to decrease with time.

There were no differences in oxygen consumption before and after ECC in group I and after ECC in group II, nor before and after anoxic arrest in group II. In the hypertrophied heart (group III, IV), there was no difference before and after ECC. Oxygen consumption tended to decrease after anoxic arrest in group IV but the decrease was not significant.

2) Cardiac performance (Table V).

There were no significant changes in any of the parameters of cardiac performance in group I. In group II, left atrial pressure rose significantly after ECC ($p < 0.001$), but the other parameters showed no significant changes. In group III, the percent change of V_{max} before and after ECC decreased significantly after ECC, but the other parameters showed no significant changes. In group IV, left ventricular enddiastolic pressure and left atrial pressure rose significantly after ECC, and the percent change of V_{max} before and after ECC decreased significantly ($p < 0.05$).

In other words, cardiac performance in group IV was most depressed, more depressed in group III and slightly depressed in group II. In group I, no depression was recognized.

3) Total and regional coronary blood flow.

a) Total coronary blood flow and blood flow to atria, ventricles and septum (Table VI, Fig. 2, 3, 4, 5).

Table VI shows significant increases ($p < 0.03 - 0.001$) of blood flow to all portions except the atria and a significant increase ($p < 0.04$) in total coronary blood flow after ECC in group I.

TABLE IV BLOOD GAS ANALYSIS IN GROUP IV

		Pre-ECC		ECC 5 min		ECC 30 min		ECC 60 min		Post-ECC	
<i>m-AP (mmHg)</i>		90.7	(7.4)	97.9	(5.0)	95.7	(6.5)	92.9	(7.1)	80.0	(5.6)
<i>PH</i>	<i>A</i>	7.322	(0.022)	7.463	(0.028)	7.320	(0.032)	7.310	(0.024)	7.232	(0.061)
	<i>V</i>	7.259	(0.028)	7.366	(0.029)	7.239	(0.034)	7.237	(0.027)	7.139	(0.070)
	<i>CS</i>	7.255	(0.018)	7.403	(0.033)	7.288	(0.034)	7.254	(0.034)	7.180	(0.066)
<i>PO₂</i> (mmHg)	<i>A</i>	303.7	(29.2) ^{*1}	315.4	(18.7)	349.2	(34.2)	261.1	(13.7)	88.6	(9.1) ^{*1}
	<i>V</i>	61.3	(2.2)	55.9	(3.2)	57.5	(4.9)	60.6	(6.1)	42.8	(6.9)
	<i>CS</i>	35.0	(4.0)	34.8	(4.2)	45.8	(7.7)	53.9	(8.7)	37.7	(5.1)
<i>PCO₂</i> (mmHg)	<i>A</i>	30.7	(2.4) ^{*2}	29.0	(2.3)	33.4	(2.8)	38.1	(3.3)	41.1	(1.8) ^{*2}
	<i>V</i>	34.4	(2.8)	34.8	(2.6)	40.7	(2.4)	43.6	(2.4)	48.0	(3.9)
	<i>CS</i>	37.6	(4.1)	35.0	(3.2)	40.0	(2.4)	43.6	(4.1)	45.9	(3.1)
<i>Hb (g/dl)</i>		11.6	(0.5)	9.7	(0.2)	9.8	(0.3)	10.2	(0.6)	12.1	(1.2)
<i>A-CS O₂ diff</i> (vol %)		6.83	(1.20)	4.14	(0.77)	4.14	(1.05)	3.14	(0.88)	5.00	(1.14)
<i>O₂ consumption</i> (ml/min/100g)		—		4.31	(1.22)	—		2.69	(0.75)	8.63	(2.07)
<i>CVP (cm H₂O)</i>		4.9	(0.5) ^{*3}	9.8	(1.2)	12.8	(1.8)	14.2	(2.5)	12.2	(1.6) ^{*3}

AP: arterial pressure A: arterial V: venous CS: coronary sinus mean (SE)

ECC: extracorporeal circulation

*1 $P < 0.001$ *2 $P < 0.0003$ *3 $P < 0.005$

During ECC, the total coronary blood flow and the blood flow to the septum and the left ventricle decreased significantly ($p < 0.04 - 0.05$) to 37–48% of the blood flow before ECC. In group II, total coronary blood flow and the blood flow to the atria, the septum, and the left ventricle after anoxic arrest trended to increase. The blood flow to the right ventricle increased significantly from 27.2 ± 5.2 ml/min./100 g to 57.7 ± 11.3 ml/min./100 g ($p < 0.04$). In group III, the total coronary blood flow and the blood flow to each chamber showed the trends as in group I and increased significantly after ECC. During ECC, they decreased to be 56–74% of the blood flow before ECC and did not decrease significantly. In group IV, the increase of the blood flow after anoxic arrest as seen in group II did not occur. After ECC, as compared the blood flow to each chamber, that to the right ventricle was the most. Such a change was not seen in the other groups.

In regard to the mean LV/RV flow ratio (Fig. 6), in group I, it decreased from 1.60 ± 0.12 to 1.31 ± 0.09 after ECC. In group II, it decreased significantly ($p < 0.05$) from 1.44 ± 0.07 (before) to 1.21 ± 0.09 after anoxic arrest and

became 1.24 ± 0.07 after ECC. In group III, it decreased from 1.50 ± 0.20 (before) to 1.32 ± 0.13 after ECC. In group IV, it was 1.25 ± 0.11 before anoxic arrest, 1.10 ± 0.18 after anoxic arrest and 1.13 ± 0.10 after ECC.

b) Left ventricular intramyocardial blood (Table VII, Fig. 7, 8, 9, 10).

In group I, the blood flow to each layer of the left ventricle changed in parallel with the total coronary blood flow. In group II, the blood flow to the inner and middle layers increased significantly ($p < 0.001 - 0.03$) after anoxic arrest. The blood flow to the outer layer increased, but not significantly. The blood flow to the inner and middle layers during ECC in group III decreased significantly ($p < 0.05$). After ECC, the blood flow to the outer layer only increased significantly ($p < 0.04$). In group IV, the blood flow to each layer did not show such changes before and after anoxic arrest seen in group II. In particular, the blood flow to the inner layer did not change.

In regard to the left ventricular Endo/Epi flow ratio (Fig. 11) which was studied because of its relationship with left ventricular performance, in group I, it was 1.46 ± 0.09 before ECC, $1.55 \pm$

Fig.2. The blood flow to atria, ventricles and septum in group I.

Fig.3. The blood flow to atria, ventricles and septum in group II.

0.24 after 60 min. of ECC and 1.08 ± 0.22 after ECC. There were no significant changes. In group II, it was 1.24 ± 0.08 after 5 mins. of ECC, 1.15 ± 0.11 after 60 mins. of and 1.20 ± 0.07 after ECC. In group III, it was 1.69 ± 0.06 before ECC, 1.46 ± 0.06 after 60 mins. of ECC and decreased significantly to 1.37 ± 0.06 after ECC ($p < 0.03$). In group IV, it was 2.02 ± 0.38 after 5 mins. of ECC, 1.63 ± 0.42 after 60 mins. of ECC and 1.35 ± 0.10 after ECC.

The Endo/Epi flow ratios trended to decrease after ECC but were more than 1.0 in all groups.

DISCUSSION

Although the LOS is a major complication of open-heart surgery, its etiology is not adequately understood. In 1967, Taber et al.¹ reported the autopsy findings that approximately 30% of cardiac muscle was affected by scattered microinfarction which, they thought, were due to small bubbles, tissue pieces, and platelet aggregation driving from the extracorporeal circuit. They cited these microinfarction as a cause of

the LOS. In 1969, Najafi et al.² reported the findings, at autopsy, of left ventricular hemorrhagic necrosis as the cause of death. This was restricted to the left ventricle and was usually seen in the subendocardium. The cause of this change, however, was unclear.

Buckberg et al.^{3,11} on the other hand, reported that subendocardial ischemia and hemorrhagic necrosis were the cause of death in the immediate post-operative period after open-heart surgery in the presence of left ventricular hypertrophy. They suggested that this subendocardial ischemia was due to a discrepancy between metabolic needs and available blood supply, the subendocardium being more prone than subepicardium to a decrease in its blood supply caused by force of contraction of the left ventricle.

The anoxic arrest used during open-heart surgery naturally causes ischemic changes in the myocardium. This leads to decreased contractility of cardiac muscle fibers.^{12,13} Iyenger et al.¹⁴ reported that, in all cases of normothermic anoxic arrest for 60–75 mins., hemorrhage and

Fig. 4. The blood flow to atria, ventricles and septum in group III.

necrosis were seen in the left ventricular sub-endocardium and that these changes were particularly marked in hypertrophied left ventricle. In fact, in heart with existing hypertrophy, the presence of hypertrophy alone makes the sub-endocardium particularly susceptible to ischemia^{15,16}

When all of these reports are taken into consideration, subendocardial hemorrhagic necrosis is obviously a prominent factor in the genesis of LOS. In this report therefore the ECC technique used clinically was used in a study of regional coronary hemodynamics in non-hypertrophied and hypertrophied hearts. Changes in cardiac performance in relation to anoxic arrest were analyzed.

1) Total coronary blood flow and cardiac performance.

Blood gas analysis of each group 60 mins. after the cessation of ECC showed acidemia and hypoxemia but the changes in all groups were of approximately the same extent. It was, therefore, that any effects due to such blood gas results

Fig. 5. The blood flow to atria, ventricles and septum in group IV.

Fig. 6. LV/RV flow ratio.

could be ignored. Decrease in cardiac performance occurred in groups III and IV (Table V). The decrease was only slight in group II and did not occur at all in group I. The changes of total

TABLE V CARDIAC PERFORMANCE

		Group I	Group II	Group III	Group IV
Cardiac index l/min/M ²	Pre-ECC	2.02 (0.24)	3.33 (0.26)	2.65 (0.34)	3.17 (0.70)
	Post-ECC	2.01 (0.39)	3.40 (0.39)	2.33 (0.21)	2.93 (0.68)
	Percent change	95.5 (13.1)	103.0 (5.5)	90.1 (5.71)	92.66 (6.16)
LVEDP (mmHg)	Pre-ECC	6.97 (0.33)	6.75 (0.67)	12.5 (1.95)	5.00 (1.48)* ¹
	Post-ECC	10.03 (3.21)	10.35 (3.54)	15.2 (3.3)	14.20 (2.69)* ¹
	Percent change	140.6 (39.8)	123.0 (29.8)	122.9 (7.1)* ²	360.0 (87.2)* ²
LAP (cm H ₂ O)	Pre-ECC	7.88 (0.85)	6.75 (0.82)* ³	6.00 (0.41)	6.14 (0.83)* ⁴
	Post-ECC	12.25 (2.04)	9.50 (1.0)* ³	7.53 (1.26)	15.21 (1.70)* ⁴
	Percent change	164.8 (28.7)	142.6 (5.9)	129.6 (18.4)* ⁵	214.1 (45.4)* ⁵
V _{max}	Percent change	95.8 (9.6)	112.6 (15.9)	89.0 (3.19)* ⁶	75.5 (8.5)* ⁷
LVSW (g·meters/M ²)	Pre-ECC	28.7 (7.1)	36.1 (3.3)	25.6 (3.2)	35.6 (6.5)
	Post-ECC	20.7 (5.0)	32.9 (5.9)	20.3 (5.5)	28.1 (6.4)
	Percent change	71.1 (7.0)	89.3 (6.8)	81.7 (10.3)	83.6 (11.1)
Heart rate	Pre-ECC	165.6 (5.4)	162.9 (6.8)* ⁸	176.3 (8.7)* ⁹	127.1 (7.9)
	Post-ECC	150.4 (8.6)	145.6 (6.8)* ⁸	143.7 (5.2)* ⁹	121.1 (15.7)

LVEDP: left ventricular enddiastolic pressure

mean (SE)

LAP: left atrial pressure LVSW: left ventricular stroke work

ECC: extracorporeal circulation

*¹ $P < 0.03$ *² $P < 0.01$ *³ $P < 0.001$ *⁴ $P < 0.05$ *⁵ $P < 0.05$ *⁶ $P < 0.01$ *⁷ $P < 0.05$ *⁸ $P < 0.03$ *⁹ $P < 0.01$

coronary blood flow in group I were significant and that in group III showed same pattern but not significant at 60 mins. after ECC. Comparison of group II and IV showed that group IV, with a total coronary blood flow of 132.9 ml/min./100 g after ECC, was less than group II and III at the same points of time, but the total coronary blood flow under beating-working conditions in the hypertrophied heart (group III) was 113.1 ml/min./100 g and the group IV results exceed this. Group IV oxygen consumption after ECC was 8.65 ± 2.07 ml/min./100g. This was not lower than the other groups and showed that at the point in time, the flow was not diminished. The decrease in cardiac performance and the changes in total coronary blood flow did not concur.

2) The blood flow to atria, ventricles and septum and LV/RV flow ratio.

In group I, the flow to each chamber during ECC was different with a significant drop in flow to the septum and left ventricle. This was probably due to the non-working state. In group III, there was a trend towards a decrease during ECC

but this was not a significant difference. In both group I and III, there was a significant increase in flow to each site after ECC compared with before ECC. In group II, immediately after anoxic arrest, there was a trend towards increased blood flow to all areas, with a particularly significant increase ($p < 0.04$) in the blood flow to the right ventricle. This was thought to be a reactive hyperemia type of reaction. In group IV, however, there were almost no changes in the blood flow to each area immediately after anoxic arrest and there were no reactive hyperemia type of responses corresponding to that seen in group II. In group II, there was a increasing tendency in the blood flow to each area after ECC compared with before ECC in group I whereas in group IV, there were no changes at all even after ECC. There were, however, no significant differences in the blood flow between group III and IV at each of the time points studied before and during ECC.

Cardiac performance and the blood flow to atria, ventricles and septum were compared. The decrease in the blood flow in group I during ECC

TABLE VI TOTAL AND REGIONAL CORONARY BLOOD FLOW

		Pre-ECC	ECC 5 min	ECC 60 min	Post-ECC
G I	atria	40.8 (5.5)		23.4 (5.4)	75.7 (14.0)
	septum	153.1 (26.8)*1 *2		55.9 (12.7)*2	184.1 (19.3)*1
	RV	67.8 (8.0)*3		39.2 (8.0)	136.1 (16.8)*3
	LV	114.0 (16.6)*4 *5		52.6 (10.6)*5	184.7 (14.3)*4
	T.C.B.F.	80.6 (12.7)*6 *7		38.3 (5.9)*7	130.9 (18.3)*6
G II	atria		17.2 (2.2)	27.7 (4.8)	94.4 (16.5)
	septum		45.0 (7.2)	83.3 (20.3)	205.8 (45.7)
	RV		27.2 (5.2)*8	57.7 (11.3)*8	144.6 (46.5)
	LV		51.4 (11.9)	77.6 (17.8)	189.4 (65.6)
	T.C.B.F.		43.2 (8.6)	77.4 (20.4)	182.3 (54.6)
G III	atria	67.8 (10.5)*9		49.9 (9.3)	115.5 (19.3)*9
	septum	118.9 (13.8)*10		66.8 (2.9)	183.2 (18.6)*10
	RV	92.8 (11.8)*11		61.6 (10.3)	170.2 (27.0)*11
	LV	133.2 (16.5)*12		75.9 (9.1)	201.9 (20.8)*12
	T.C.B.F.	113.1 (8.1)*13		65.6 (4.5)	180.0 (20.7)*13
G IV	atria		41.1 (8.6)	51.8 (5.2)	88.8 (13.6)
	septum		75.5 (11.7)	91.8 (17.1)	134.0 (22.7)
	RV		74.9 (15.2)	97.9 (26.1)	153.3 (31.1)
	LV		83.6 (14.6)	95.1 (16.0)	145.2 (19.6)
	T.C.B.F.		73.3 (11.6)	94.2 (16.6)	132.9 (21.2)
ml/min/100g					
RV: right ventricle LV: left ventricle T.C.B.F.: total coronary blood flow		mean (SE)			
ECC: extracorporeal circulation					
*1 P < 0.03		*2 P < 0.04	*3 P < 0.001	*4 P < 0.01	
*5 P < 0.05		*6 P < 0.04	*7 P < 0.05	*8 P < 0.04	
*9 P < 0.05		*10 P < 0.05	*11 P < 0.05	*12 P < 0.04	
*13 P < 0.04					

was due to the non-working beating state and it was considered that this decreased blood flow did not cause any damage to the myocardium. In group II, increased flow to each area after anoxic arrest indicated that payment of the oxygen debt incurred during anoxic arrest took place satisfactorily. In group III, the significant decrease in the flow to each area seen in group I during ECC did not occur, moreover, the flow after the cessation of ECC was increased compared with that during it. In other words, there were no exact changes at all in intracardial coronary blood flow in group III that could explain the decrease in cardiac performance after ECC. In group IV, there was no increase in flow to each area after anoxic arrest (as seen in group II) and it was possible that the oxygen debt after anoxic arrest was not adequately repaid. This point may help to explain the decrease in cardiac performance in

group IV.

In regard to the LV/RV flow ratio, Hottenrott et al.¹⁷ reported that, in the normal heart under beating-working conditions, the ratio was 1.49 but that it fell significant to 0.94 during beating-nonworking conditions. They explained this by the fact that, since external work is zero, both ventricles receive approximately equivalent blood flows. Furthermore, at the time of fibrillation, the LV/RV flow ratio decreases even further and the flow to left ventricle decreases. In group II, there was a significant drop at the time of anoxic arrest ($p < 0.05$). The value for group II after ECC was significantly lower ($p < 0.03$) than the control value for group I before ECC. There were no significant differences between the values for group III before ECC and group IV after ECC. Therefore, the LV/RV flow ratio showed no relation to the fall in cardiac

TABLE VII LEFT VENTRICULAR INTRAMYOCARDIAL CORONARY BLOOD FLOW

		Pre-ECC	ECC 5 min	ECC 60 min	Post-ECC
G I	inner layer	128.2 (21.4)* ¹		69.9 (18.9)* ¹	186.0 (25.4)
	middle layer	122.9 (17.9)* ² * ³		48.3 (8.1)* ²	186.6 (18.7)* ³
	outer layer	97.1 (12.1)* ⁴ * ⁵		48.5 (6.8)* ⁴	183.3 (22.4)* ⁵
G II	inner layer		57.5 (12.9)* ⁶	92.5 (29.0)* ⁶	206.9 (62.8)
	middle layer		55.1 (13.2)* ⁷	71.9 (15.6)* ⁷	139.7 (10.7)
	outer layer		51.8 (13.5)	66.3 (13.7)	163.7 (48.7)
G III	inner layer	172.2 (26.3)* ⁸		87.0 (10.2)* ⁸	237.7 (25.6)
	middle layer	148.4 (17.7)* ⁹		77.0 (8.8)* ⁹	211.1 (18.3)
	outer layer	102.2 (14.7)* ¹⁰		63.8 (10.7)	170.8 (23.1)* ¹⁰
G IV	inner layer		122.2 (13.5)	112.6 (23.0)	176.2 (26.5)
	middle layer		89.2 (20.2)	92.8 (16.0)	154.6 (20.1)
	outer layer		55.9 (9.8)	71.0 (12.1)	116.3 (14.6)

ml/min/100g

ECC: extracorporeal circulation

*¹ $P < 0.05$ *⁵ $P < 0.001$ *⁹ $P < 0.05$ *² $P < 0.01$ *⁶ $P < 0.03$ *¹⁰ $P < 0.04$ *³ $P < 0.02$ *⁷ $P < 0.001$

mean (SE) ml/min/100

*⁴ $P < 0.02$ *⁸ $P < 0.05$

Fig. 7. Left ventricular intramyocardial blood flow in group I.

Fig. 8. Left ventricular intramyocardial blood flow in group II.

Fig.9. Left ventricular intramyocardial blood flow in group III.

Fig.10. Left ventricular intramyocardial blood flow in group IV.

Fig.11. Left ventricular Endo/Epi flow ratio.

performance or to the extent of the fall.

3) Intramyocardial blood flow in left ventricle and left ventricular Endo/Epi flow ratio.

The changes in circumference of the various layers of the left ventricular wall during systole are reported to be 20% in inner layer, 12% in middle layer, and 5% in outer layer.¹⁸ Based on this report, the oxygen requirements of the inner layer must be more than the requirements of the outer layer. Gamble et al.¹⁹ reported that the oxygen saturation of subendocardial veins was lower than the oxygen saturation of subepicardial veins. In short, it appears that the supply of oxygen to the inner layer depends on the extent of oxygen dissociation and the volume of blood flow.

The blood flow to each of the three layers in group I decreased significantly during ECC but, in comparison to the flow before ECC, only the flow to middle and outer layers increased significantly after ECC.

In group II, the blood flow to the middle and inner layers after anoxic arrest, when compared with before anoxic arrest, increased significantly. This was a reactive hyperemia type of reaction, the increase being for payment of the oxygen debt incurred during anoxic arrest. The mechanism of control of blood flow in blood vessels of the inner and middle layers of the left ventricle in group II includes responsiveness to the meta-

bolic needs of the myocardium. In the experiments of Codd et al²⁰ also, the percentage of blood flow going to the left ventricle after 30 min. of anoxic arrest decreased but the percentage going to the left ventricular endocardium and papillary muscle showed either no change or an increase. Ischemia of the subendocardium thus was not detected.

In group III, the flow to the left ventricle during ECC did not decrease significantly but the flow to the inner and middle layers showed a significant decrease. This decrease is a problem when considered in the light of the decrease in cardiac performance after ECC but in view of the fact that the Endo/Epi flow ratio at the same time was 1.46 and the heart was in a non-working beating state, underperfusion of the inner layer is inconceivable. Baird et al²¹ studied myocardial blood flow and intramyocardial pressure in the hypertrophied heart. When the perfusion pressure was 80 mmHg, the Endo/Epi flow ratio was 1.07 and the subendocardium did not develop ischemia. After ECC, the Endo/Epi ratio was 1.37 and there was no underperfusion of the inner layer. In summary, therefore, the decrease in cardiac performance after ECC in group III was not due to any abnormality of myocardial blood flow within the left ventricle; that is, it is not due to underperfusion and ischemia of the subendocardium.

In group IV, after anoxic arrest, there was no increase in blood flow to any of the three layers and there was no response corresponding to the reactive hyperemia type reaction seen in the non-hypertrophied heart. When the number of capillaries per unit area in hypertrophied heart (normal heart; 3,700/cm², hypertrophied heart; 1,800/cm²)²² is taken into account, it would appear that, during ECC, the blood vessels of the left ventricle, especially of the inner layer, have dilated to the fullest extent and reached the limit of their reserve. Therefore, it is probable that payment of the oxygen debt incurred during anoxic arrest is inadequate. The Endo/Epi ratio, however, was always greater than 1.0 at all three points of time. The lack of any increase in blood flow to the inner layer after anoxic arrest was possibly a causative factor in the decrease in cardiac performance, but it is important to determine whether any discrepancy exists between available blood flow and the metabolic needs of inner layer; that is, a better understanding of the cellular metabolism of the myocardium of the inner layer is necessary.

SUMMARY

It was researched how the ECC affects on cardiac performance and the total and regional coronary blood flow, using two groups of dogs with a hypertrophied heart and a non-hypertrophied heart, each group of which was further divided into two subgroups depending on whether the intermittent 40 mins. anoxic arrest was applied or not. Cardiac performance before and 60 mins. after cessation of ECC were compared each other. Coronary hemodynamics was studied before, during (immediately before and after anoxic arrest), and 60 mins. after cessation of ECC, using 15 ± 5 diameter radioactive microspheres.

1) In the group of a non-hypertrophied heart, no obvious changes of cardiac performance were seen before and after ECC. The total coronary blood flow increased after ECC than before. Though the regional coronary blood flow pattern showed no differences in this group except only immediately after anoxic arrest, when the regional blood flow into the right ventricle, inner and middle layers of the left ventricle increased.

2) In the group of a hypertrophied heart, cardiac performance decreased after ECC, and further significant decrease was observed in the subgroup of anoxic arrest. No significant changes of the total coronary blood flow were observed before and after ECC in this group, even when compared with that in the group of a non-hypertrophied group. However, the increase of blood flow to the right ventricle, inner and middle layers of the left ventricle immediately after anoxic arrest was not observed, that was seen in the group of a nonhypertrophied heart.

3) It follows that the decrease of cardiac performance after ECC in the group of a hypertrophied heart is not due to the changes of the total and regional coronary blood flow. It is considered that the difference of the regional coronary blood flow pattern changes immediately after anoxic arrest between the non-hypertrophied heart group and hypertrophied group may cause the different changes of cardiac performance before and after ECC between the two groups.

This consideration should be more justified by evaluating not only coronary hemodynamics but also the relationship between cardiac metabolic needs and the regional coronary blood flow.

Acknowledgement

The author wishes to express his profound thanks to Prof. Shigeru Teramoto for his kind guidance, to Yoshimasa Senoo, M. D. for his helpful advice and encouragement, and to Shunji Kawakami, M. D., Yorikazu Nakayama, M. D. and Kazuhide Aokage, M. D. for their kind assistance.

REFERENCES

1. TABER, R. E., MORALES, A. R., & FINE, G.: Myocardial necrosis and postoperative low-cardiac-output syndrome. *Ann. Thorac. Surg.* 4: 12, 1967.
2. NAJAFI, H., HENSON, D., DYE, W. S., JAVID, H., HUNTER, J. A., CALLAGHAN, R., EISENSTEIN, R., & JULIAN, O. C.: Left ventricular hemorrhagic necrosis. *Ann. Thorac. Surg.* 7: 550, 1969.
3. BUCKBERG, G. D., FIXLER, D. E., ARCHIE, J. P., & HOFFMAN, J. I. E.: Experimental subendocardial ischemia in dogs with normal coronary arteries. *Circ. Res.* 30: 67, 1972.
4. OKADA, K., KOSUGI, I., KITAGAKI, T., YAMAGUCHI, Y., YOSHIKAWA, Y., KAWAKAMI, S., & SENOO, Y.: Pathophysiology of shock. *Jpn. Circ. J.* 41: 346, 1977.
5. HERRMANN, G. R.: Experimental heart disease. I. Methods of dividing hearts; with sectional and proportional weights and ratios for two hundred normal dogs' hearts. *Am. Heart J.* 1: 213, 1925.
6. MASON, D. T., SPANN, J. F., & ZELIS, R.: Quantification of the contractile element shortening determined by the instantaneous relation between the rate of pressure rise and pressure in the left ventricle during isovolemic systole. *Am. J. Cardiol.* 26: 248, 1970.
7. RUDOLPH, A. M. & HYNEMANN, N. A.: The circulation of the fetus in utero. Methods for studying distribution of blood flow, cardiac output and organ blood flow. *Circ. Res.* 21: 163, 1967.
8. SENOO, Y., TAKAHASHI, S., EBARA, Y., TERAMOTO, S., KASAI, T., KAWAKAMI, S., KOSUGI, I., YAMAGUCHI, Y., & OKADA, K.: Distribution of systemic blood flow during normothermic cardiopulmonary bypass. *J. Japan. Associat. Thorac. Surg.* 24: 199, 1974.
9. BUCKBERG, G. D., LUCK, J. C., PAYNE, D. B., HOFFMAN, J. I. E., ARCHIE, J. P., & FIXLER, D. E.: Some sources of error in measuring regional blood flow with radioactive microsphere. *J. Applied Physiol.* 31: 598, 1971.
10. UTLEY, J., CARLSON, E. L., HOFFMAN, J. I. P., MARTINEZ, H. M., & BUCKBERG, G. D.: Total and regional myocardial blood flow measurements with 25 15 9 and filtered 1-10 diameter microspheres and antipyrine in dogs and sheep. *Circ. Res.* 34: 391, 1974.
11. BUCKBERG, G. D., TOWERS, B., PAGLIA, D. E., MULDER, D. G., & MALONEY, J. V.: Subendocardial ischemia after cardiopulmonary bypass. *J. Thorac. Cardiovasc. Surg.* 64: 669, 1972.
12. ENRIGHT, L. P., STAROSCIK, R. N., & REIS, R. L.: Left ventricular function after occlusion of the ascending aorta. *J. Thorac. Cardiovasc. Surg.* 60: 737, 1970.
13. BENING, G., HELMSWORTH, J., STOCKERT, J., & KAPLAN, S.: Human myocardial performance during surgical treatment of cardiac defect. *J. Thorac. Cardiovasc. Surg.* 59: 800, 1970.
14. IYENGER, S. R. K., RAMCHAND, S., CHARRETTE, E. J. P., & LYNN, R. B.: An experimental study of subendocardial hemorrhagic necrosis after anoxic arrest. *Ann. Thorac. Surg.* 13: 214, 1972.
15. OKUMORI, M.: The intramyocardial tissue pressure and the regional myocardial blood flow in experimentally produced left ventricular hypertrophy. Its surgical significance. *J. Japan. Associat. Thorac. Surg.* 23: 251, 1975.
16. VINCENT, W. R., BUCKBERG, G. D., & HOFFMAN, J. I. P.: Left ventricular subendocardial ischemia in severe valvar and supra-valvar aortic stenosis. A common mechanism. *Circulation* 49: 326, 1974.
17. HOTTENROTT, C., MALONEY, J. V. Jr., & BUCKBERG, G. D.: Studies of the effects of ventricular fibrillation on the adequacy of regional myocardial flow. I. Electrical vs. spontaneous fibrillation. *J. Thorac. Cardiovasc. Surg.* 68: 615, 1974.
18. SONNENBLICK, E. H.: Correlation of myocardial ultrastructure and function. *Circulation* 38: 29, 1968.
19. GAMBLE, W. J., LaFARGE, C. G., FYLER, D. C., WEISUL, J., & MONROE, R. G.: Regional coronary venous oxygen saturation and myocardial oxygen tension following abrupt changes in ventricular pressure in the isolated dog heart. *Circ. Res.* 35: 672, 1974.
20. CODD, J. E., HAHN, J. W., JELLINEK, M., MENZ, L. J., & WILLMAN, V. L.: Distribution of myocardial blood flow during extracorporeal circulation. *J. Surg. Res.* 19: 183, 1975.
21. BAIRD, R. J., DUTKA, F., OKUMORI, M., de la ROCHA, A., GOLDBACH, M. M., HILL, T. J., & MacGREGOR, D. C.: Surgical aspects of regional myocardial blood flow and myocardial pressure. *J. Thorac. Cardiovasc. Surg.* 69: 17, 1975.
22. ROBERT, J. T.: Development and structure of the cardiovascular system. McGraw-Hill Books. 1961.